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PRINCIPAL INVESTIGATOR:	Dr. W. Geoffrey Wright
CONTRACTING ORGANIZATION:	TEMPLE UNIVERSITY-OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION Philadelphia, PA 19122
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Dr. W. Geoffrey Wright

E-Mail: wrightw@temple.edu

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Temple University – Of the Commonwealth System of Higher
1801 N. Broad Street
Philadelphia, PA 19122-6003

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14. ABSTRACT
The project has validated a technologically advanced, yet portable system, which will be beneficial to deployed warfighters and clinical military personnel. The device can be used to provide a quick assessment of physiological processes involved in postural control, which will assist with clinical screening of traumatic brain injury (TBI). Knowledge of acute symptoms associated with TBI can help clinicians make important decisions regarding treatment and/or return to duty. Early identification of motor symptoms caused by TBI will help expedite full recovery of service members to pre-injury health. The research plan involves a novel combination of virtual reality (VR) technology with intensive balance challenges performed on a modified Wii Balance Board. *Implementation of this device will enhance current approaches in TBI and mild TBI (i.e. concussion) diagnosis and rehabilitation management* with high relevance to the military and general population (e.g. sports concussion). One of the final products of the project includes a new device and software user-interface that has been tested and validated relative to a high-quality research-grade forceplate and we tested clinical concurrent validity of device relative to clinical criterion-measures (Neurocom SOT and BESS). Normative values on healthy civilians and military, and concussed individuals were tested. Military test sites that were completed included multiple USCG stations and the Naval Post-Graduate School.

15. SUBJECT TERMS
Traumatic brain injury (TBI), Blast-induced TBI, concussion, balance assessment, virtual reality, field-deployable, novel technology

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1. INTRODUCTION

The purpose of this study was to validate and test the reliability of the Virtual Environment Traumatic Brain Injury (TBI) screen (VETS) protocol in measuring standing balance. This system consists of software, a Wii balance board, an Airex foam pad, and a large screen television that can be used to measure balance in healthy or neurologically impaired individuals. Results from this project have validated that the VETS protocol is a valid tool to help improve sensitivity and specificity to balance related changes in service members with blast-related or blunt-force TBI or athletes with concussion. The deliverable is an affordable, user-friendly, portable (i.e. field-deployable) protocol that requires minimal training and expertise to utilize. This product will help reduce risk to military personnel (and athletes) who have experienced a mild TBI by accurately assessing their recovery thus reducing the likelihood that they will be prematurely returned to duty (or returned to play). The likelihood of a second head trauma is increased during the recovery period and repeat traumas present an even greater danger than initial injury (Kelly et al 1991; Langlois et al 2006). A second separate set of aims led by Dr. Richard Servatius was added to the existing contract by CAPT Jack Tsao USN (ret) for the purposes of an on-going project being carried out at USCG stations across the country, with a primary goal of investigating the interaction of PTSD with TBI in service members by focusing on neuromotor and neurobehavioral assessments and epigenetic predictors. The VETS protocol was tested on a cohort of USCG service members in coordination with that existing project. The addition of funds in year 2 to the existing CDMRP contract were earmarked for Dr. Servatius' team to support analysis and preparation of the findings for the USCG project.

2. KEY WORDS

Concussion, mild traumatic brain injury (mTBI), post-traumatic stress disorder (PTSD), Virtual Reality, field-deployable, balance, Sensory Organization Test, Balance Error Scoring System, diagnosis, rehabilitation

3. ACCOMPLISHMENTS

This section of the report shall describe the research accomplishments associated with each task outlined in the approved Statement of Work.

Major Task 1: Institutional Review Board Application and Approval

Subtask 1: Prepare Regulatory Documents and Research Protocol for Project

- ☑ Refine eligibility criteria, exclusion criteria, screening protocol
- ☑ Finalize consent form & human subjects protocol
- ☑ Coordinate with Sites for IRB protocol submission
- ☑ Coordinate with Sites for Temple University IRB review
- ☑ Coordinate with Sites for Military 2nd level IRB review (ORP/HRPO)

☑ *Milestone Achieved:* Local IRB approval at Temple
☑ *Milestone Achieved:* HRPO approval for all protocols for Temple
☑ *Milestone Achieved:* An existing IRB at Naval Hospital Camp Lejeune (NHCL) that

Dr. Servatius had already had approved was modified to include balance assessment. This IRB expired while awaiting an MOU to be signed off by NHCL command staff. In the mean time NHCL has begun developing its own independent IRB which is undergoing review and will become active this year. Our IRB for the Intrepid Spirit Concussion Recovery Center, Camp Lejeune, NC, which falls under the umbrella of NHCL will be re-submitted at that point.

Subtask 2: Validate Wii™ Balance Board relative to NeuroCom forceplate

☑ Running Wii Balance Board validation protocol.

☑ *Milestone Achieved: Wii Balance Board validated relative to Neurocom SOT and integrated with VETS*

Subtask 3: Usability optimization of VETS human-computer interface

☑ Computer programmer and RA's work with senior investigators to integrate new equipment and software with online analysis programs and virtual environments

☑ *Milestone Achieved: Optimized VETS protocol ready for validation in Task 3-5*

Major Task 2: Preparation for human subject testing

Subtask1: Hiring and Training of Study Staff Advertise and interview for computer programmer

☑ Computer programmer hired and began optimization in October

☑ Advertise and interview for research assistants (RA) – Two RA's hired

☑ Coordinate with Sites for training study personnel on BESS and ImPACT to ensure high level of concordance among raters

☑ *Milestone Achieved: Project staff selected and trained*

Subtask 2: Validate Wii™ Balance Board relative to NeuroCom forceplate

☑ Running Wii Balance Board validation protocol.

☑ *Milestone Achieved: Wii Balance Board validated and integrated into VETS protocol*

Subtask 3: Usability optimization of VETS human-computer interface

☑ Computer programmer and RA's work with senior investigators to integrate new equipment and software with online analysis programs and virtual environments

☑ *Milestone Achieved: Optimized VETS protocol. New releases with added features will be an on-going objective.*

Major Task 3: Data Collection on healthy student population at Temple University

Subtask 1: Validate VETS relative to BESS and SOT for healthy subjects

☑ Implemented multiple recruitment tactics including, but not limited to: online promotion of study, website links, and print advertisement for healthy volunteers

☑ Completed running of 60 healthy civilian participants through the VETS, BESS, SOT validation protocol in 3 test sessions each (180 test sessions total) plus 33 healthy civilian athletes in 1 test session

☑ Processed to establish norms for healthy population on VETS protocol

☑ *Milestone Achieved: Healthy norms established for VETS, BESS, SOT.*

Major Task 4: Data Collection on athlete population from Temple Concussion Program

Subtask 1: Validate VETS relative to BESS and SOT for concussed subjects

☑ Implemented multiple recruitment tactics including, but not limited to: online promotion of study, website links, and print advertisement for concussed volunteers

☑ Scheduled and ran of participants through the VETS, BESS, SOT validation protocol for 34 concussed subjects in three test sessions

☑ Compared healthy norms to injured population on VETS protocol

☑ Compared healthy norms to injured population on SOT protocol

☑ *Milestone Achieved:* Compared the mTBI cohort for VETS, BESS, SOT to the healthy norms and determined that VETS protocol is highly sensitive (81.8%) and specific (85.7%). To further validate the VETS protocol across a wide range of time-since-injury, i.e. acute, subacute, chronic, we compared a stratified sample.

Major Task 5: Data Collection on military service personnel at CG Stations

Subtask 1: Validate VETS relative to BESS for healthy military subjects

☑ Recruitment of healthy military volunteers

☑ Scheduling and running of participants through the VETS and BESS protocol for healthy subjects

☑ Data processed and established norms for healthy military population on VETS protocol and BESS

☑ *Milestone Achieved:* Established healthy norms for VETS in military population. To supplement the USCG cohort, a cohort of USN service members were collected at the Naval Post-graduate School.

Major Task 6: Data Collection on military service personnel at Naval Hospital Camp Lejeune (NHCL)

Subtask 1: Validate VETS relative to BESS for injured military with mTBI

☑ Recruitment of injured military with mTBI

□ Scheduling and running of participants through the VETS and BESS protocol for healthy subjects

□ Data processing and compare to healthy norms on VETS protocol and BESS

□ *Milestone Ongoing:* As of September 2016, an MOU has been signed and CAPT Johnson, director of Intrepid Spirit Concussion Recovery Center (ISCRC), has agreed to be site-PI for three projects that were initiated by Dr. Wright, Dr. Servatius, and Dr. Christine Marx. These projects will add to the multi-site testing of the VETS protocol on military personnel and help accomplish our goal of testing a military TBI population.

Major Task 7: Data Analysis and Report Writing

Subtask 1: PI coordinate with Sites for monitoring data collection rates and data quality

☑ Performed all analyses using common algorithms, shared output and findings with all investigators.

☑ Working with each site with dissemination of findings (abstracts, presentation, publications, DOD).

☑ *Milestone Achieved:* We have published three papers with four more submitted or in prep, presented at a dozen conferences, and submitted 12 quarterly and/or annual reports to the CDMRP.

Additional Specific Aims

Posttraumatic stress disorder (PTSD) is a major mental health problem for active military and veterans. The sources of stress, whether military or nonmilitary experiences, and their relationship to individual differences may provide important insights toward adjustment.

1) Collect in Coast Guard, USN, and USMC personnel at various stations scale data of PTSD focusing on military (PCLM) and nonmilitary (PCLNM) experiences.
2) Compare the degree of symptom clusters expressed in PCLM and PCLNM.
3) Relate PCLM and PCLNM to individual differences (sex, marital status).
4) Compare the degree of persistence of symptom clusters in PCLM and PCLNM.

A second separate set of aims was added to the existing contract (W81XWH-13-C-0189) for the purposes of supporting a project that started prior to 2013 which was not part of the original CDMRP project. This on-going project was led by Dr. Richard Servatius and CAPT Jack Tsao USN (ret) and was carried out at USCG stations across the country, with a primary goal of investigating the interaction of PTSD with TBI by focusing on neuromotor and neurobehavioral assessments and epigenetic predictors. The VETS protocol was tested on a cohort of USCG service members in coordination with that existing project. The addition of funds in year 2 to the existing CDMRP contract was used to support analysis and preparation of the findings for the USCG project. It was funded by sources other than CDMRP, so data collection had started before the CDMRP contract began. However, because CDMRP will, in part, be funding data analysis/interpretation/publication, a data usage agreement (DUA) to get access to the de-identified Coast Guard data was set up between Temple University, Syracuse VA, and SMBI.

Major Task 1: Institutional Review Board Application and Approval

Subtask 1: Prepare Regulatory Documents and Research Protocol for USCG Project

☑ Refine eligibility criteria, exclusion criteria, screening protocol
☑ Finalize consent form & human subjects protocol
☑ Coordinate with Sites for USCG IRB approved under separate project
☑ Under Review - Military 2nd level IRB review (ORP/HRPO) of site IRBs for data analysis
☑ Submit amendments, adverse events and protocol deviations as needed

De-identified data has been analyzed under the sub-contract held by Dr. Servatius. A DUA has been fully executed between all involved sites and IRB and HRPO approval for data analysis was received. Three manuscripts have been prepared and awaiting USCG approval to be submitted for peer-review.

Subtask 2: Prepare Regulatory Documents and Research Protocol for NHCL and Intrepid Spirit Concussion Recovery Center Project

☑ Refine eligibility criteria, exclusion criteria, screening protocol
☑ Finalize consent form & human subjects protocol
☐ Ongoing - Coordinate with Sites for NHCL IRB protocol submission
☐ Under Review - Coordinate with Sites for Military 2nd level IRB** review (ORP/HRPO)
☐ Submit amendments, adverse events and protocol deviations as needed

Subtask 3: Prepare Regulatory Documents and Research Protocol for Naval Medical Center San Diego

☑ Refine eligibility criteria, exclusion criteria, screening protocol
☑ Finalize consent form & human subjects protocol
☐ Ongoing - Coordinate with Sites for NMCSD IRB protocol submission
☐ Coordinate with Sites for Military 2nd level IRB** review (ORP/HRPO)
☐ Submit amendments, adverse events and protocol deviations as needed

Because a signed MOU and site IRB were successfully achieved at NHCL, current efforts are being focused on NHCL rather than NMCSD.

Key Research Accomplishments

- Wii Balance Board validated and integrated into VETS protocol. Two versions – VETS Legacy and VETS 1.0 through VETS 1.4
- VETS protocol tested for reliability and usability.
- Defined Common Data Elements (CDE) for Federal Interagency TBI Research (FITBIR) Informatics System, established multiple new CDE's for FITBIR. Uploaded 87 GUIDs
- Began collecting data on VETS, BESS, Neurocom SOT, and vestibulo-ocular/oculo-motor tests, which have recently been shown to be sensitive to the effects of mTBI (McDevitt et al, 2016; Cheever et al, *submitted*)
- Local IRB approval at Temple. Received HRPO approval for Temple protocol.
- Recruited and tested 126 participants at Temple University and conducted 284 test sessions. Healthy civilian cohort completed (n=92). Adequately powered civilian concussed cohort (n=34) achieved. Excellent accuracy was found with the VETS protocol (see Wright et al 2016 – Appendix 4)
- Established collaboration with East Stroudsburg University (ESU), run by former project coordinator, Dr. Jane McDevitt, for collaboration in multi-site testing to increase external validity and allow for stratified cohort analysis. Local IRB approval was received to initiate testing.
- Data on 53 services members without mTBI were collected and analyzed to establish healthy military norms.
- Data on 240 subjects at US Coast Guard sites was collected prior to the CDMRP contract using other funding sources. This arm of the project (See "Additional aims" SOW) was led by Dr. Richard Servatius and includes healthy service members as well as individuals with PTSD and/or mTBI. Funding from this CDMRP contract supported data analysis, interpretation, and dissemination. Three manuscripts, two

conference presentations, and one technical report were completed and ready for submission.

- Coordinated with all test sites to training study personnel on VETS, BESS and SOT to ensure high level of concordance among raters.
- Added new lab group as subcontractor to help with military group recruitment (Dr. Richard Servatius)
- Established subcontract with co-PI (LT Jay Haran), who outsourced military data collections to US Coast Guard and US Naval Hospitals. An MOU was signed by Naval Hospital Camp Lejeune and DUA between Syracuse VA and Temple University, which has led to three new research proposals to be run in the Intrepid Center for Concussions.
- Published six peer-reviewed papers, one manuscript under review, six in preparation or ready for submission.
- Presented findings at 15 conferences/meetings.
- Eight new grant applications related to military TBI with three funded and three under review.
- Significant career advancements for seven members involved in the project.

Written Narrative of Device Development and Findings

The device that we designed and validated in this project is the Virtual Environment TBI Screening (VETS) protocol (Fig 1).

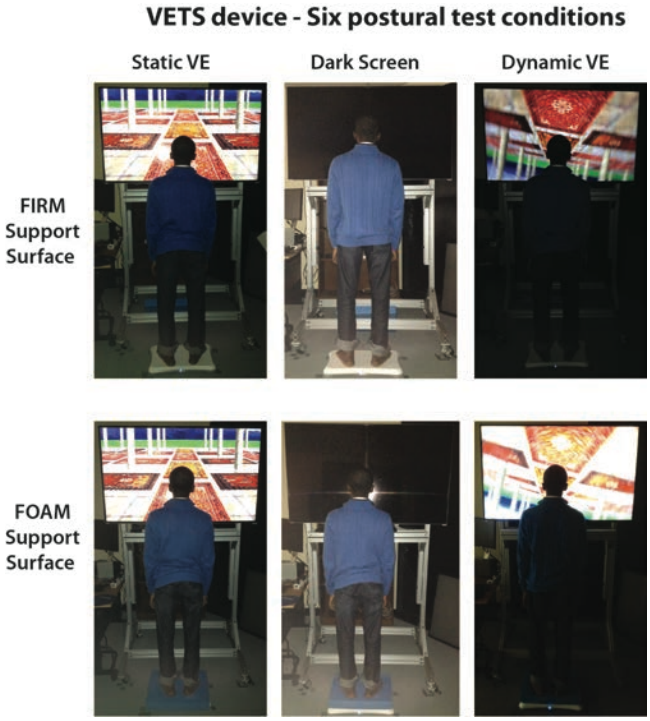

Figure 1. VETS – A VR-based balance device tests six conditions. Top row shows firm support conditions and the bottom row shows the foam support conditions. From left to right, the three columns are EO viewing a static VE scene, EC in front of a dark screen, and EO viewing a dynamic rotating scene.

The VETS protocol code has been written, and the system has been validated. We specifically compared our user interface (See Appendix 1) with the Wii Balance Board (WBB) to a high-end research grade force plate (Neurocom/Natus and AMTI) and showed that we can collect data at 100 Hz with high test-retest reliability and excellent concurrent validity (Fig. 2). This software solution that our team designed has more capability and fidelity than any existing solution available using the WBB.

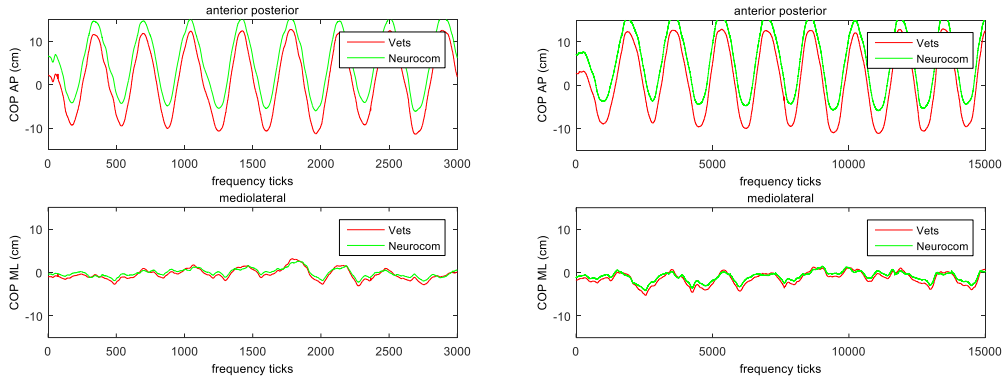

Fig 2. Two trials (left and right) each showing two traces of center of pressure in the anterior-posterior direction (upper) and mediolateral direction (lower). The subject was instructed to sway back and forth in the AP direction, while standing on the VETS controlled WBB (red), which had been placed on the Neurocom forceplate (green). Even without center aligning the forceplates, a high correlation between them was found. ICC's between VETS and NeuroCom were above 0.90 (min: 0.901, max: 0.995, $p<0.01$)

A full technical description of the device design and a user manual are included in the Appendix, but briefly the VETS device is a visual scene renderer and a data capture and recording engine. VETS operates through a multi-component system that communicates with each other as well as handling individual jobs. Below these components, and the jobs and functions they perform, as well as list any externally developed libraries (i.e. dependencies) that the components themselves may require are described. Below is the general procedure that a tester will take in use of the program, and the overall communication and state of the VETS system.

i. Upon loading and starting the program, VETs uses the WiimoteLib to facilitate a blue-tooth connection between the VETs and the Wii Balance Board.
    a. WiimoteLib is an open-source library design to allow a PC to communicate and use Wii blue-tooth based hardware. For more information, see the following website. (https://wiimotelib.codeplex.com/). This library allows real-time streaming of the center of pressure (CoP) data as a time series with a set sampling rate.

ii. Users are greeted with the Live Mode component; this is used to test if the Wii Balance Board is properly connected to the VETS systems and working, and provides a real time display of the data being received (Fig 3, upper left).

iii. Users then select to the Settings component (Fig 3, upper right). This component allows users to set up a list of the conditions to be run. Conditions are separated

into two major parts, visual and physical. Once components are selected they are stored in a Trials array list.

a. The visual parts determine if the scene is rendered as a still image ('Eyes open'), not rendered at all ('Eyes closed'), or if the scene is rendered and rotating ('Dynamic')
b. The physical parts determine if the protocol involves the use of a foam padding for the participant to stand on. Though not involved in data-gathering, this is used to help sort and organize the data for later readability.

iv. Users then select the Play component (Fig 3, lower left). This component allows users to set up the specifics of the test as a whole. These options include the Participant's Name, the Session Name, the Sampling Rate (locked at 100 in future versions), the time given to wait between conditions, and the running time of each condition. When a user is ready they can select "Run Animation" and this proceeds to the Simulation component. The Simulation component reads in the earlier created Trials array list, and splits the program off into three asynchronous systems.

a. The major Simulation component handles the renderer and control of the conditions. It will run through the Trials array, rendering the scene and passing the individual details to all other involved components. This is the main render engine and is one of the heavier components in the system.
b. RecordingService runs in the background and records the WiiBB data at a rate of 100hz. This data is stored into two separate object arrays. PointF is a native WiimoteLib structure that stores the X and Y data of a point. TimedPoint is a structure that mirrors PointF but adds in Time data as well, allowing for a timeline of the recording. This data is later passed to the WritingService.
c. WritingService runs in the background and receives data from both the RecordingService and the major Simulation component. It receives from the Simulation component the protocol-type and creates a directory based on the participant name, session name, and from the RecordingService the TimedPoint data. Once it has this data it begins to write out to two different log files. A .xml log file importable into Excel, and a raw data file that just contains the values.
d. On completion of a write, AnalysisService is run on the XML, this provides descriptive statistics of the collected data, which is used in the Results Component.

v. Upon completion, user is returned to the Results component (Fig 3, lower right). Here they can select from a list all participants and session names. The component uses the data from the XML to build charts containing mathematical and statistical analysis of the data, as well as offers an Export function to export this data into a clean and easy to read format.

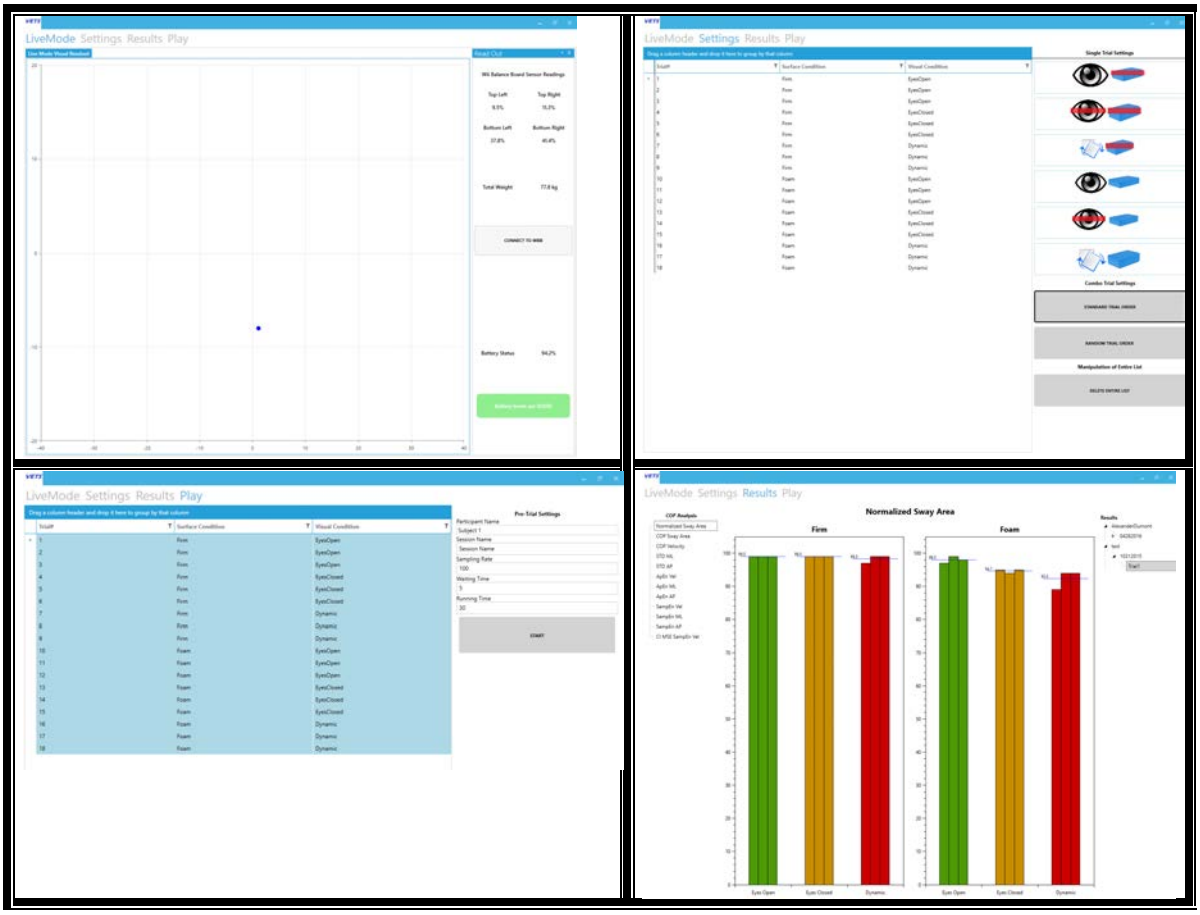

Figure 1. VETS user interface. (*Upper left*) LiveMode screen – View seen if VETS program that has successfully paired to a WBB. The plotting domain now reveals a dot that refreshes every 100 ms, representing the actual sensed center of pressure on the plate in cm. (*Upper right*) Settings screen - the user can specify individual trials desired, or use the two presets at the bottom right of the screen to select standard or randomized 18 trials. (*Lower left*) Play screen - the user can specify the Participant Name, Session Name, Sampling Rate, Waiting Time between the trials and Running Time for the trial. If any of theses text boxes are left empty, the user will not be able to click on START. The data entered in the text boxes will be the basis for storing the information and data on the tree source used in the results menu. (*Lower right*) Results screen - on the right side the Results menu-tree will automatically show up with subject and session data and on the left side various metrics can be displayed.

Human subjects testing

We created 87 GUID IDs for FITBIR. This was an 18-month process that required adapting to numerous changes in regulations by FITBIR, however, our lab manager (Dr. Jane McDevitt) successfully uploaded demographic, BESS, and SOT data to FITBIR database. We were the first group to successfully accomplish this and our involvement allowed FITBIR to test and develop their user interface.

There were 126 subjects recruited at Temple University. Military data collected at the Naval Post-Graduate School included 15 service members tested twice with one-week separation between tests and at USCG stations 38 service members were each tested

once. In total we have run 289 (221 civ + 68 mil) test sessions. We have completed all data collection on the healthy civilian cohort at Temple University.

Civilian testing
Session 1 (baseline): 126 total (92 healthy and 34 concussed subjects)
Session 2 (2 week follow-up): 84 total (54 healthy and 30 concussed subjects)
Session 3 (6 week follow-up): 74 total (52 healthy and 22 concussed subjects)

No drops outs due to adverse events, however the attrition of nine healthy and four concussed participants occurred after completion of the first session due to failure to show up for the 2-wk or 6-wk follow-up sessions. Data was successfully collected on these 13 non-compliant participants in at least 1 test session.

Current results from VETS protocol validation can be found in the two publications in the Appendix (Wright et al 2015; 2016). A summary of these results follow (see Fig. 4 and Tables 1-4). Discriminant validity was tested for the VETS on concussed subjects relative to healthy controls and was shown to be highly sensitive in the dynamic visual conditions.

Tests of VETS protocol over the multiple test sessions (baseline, 2 weeks, 6 weeks) showed significant between health-group difference ($F=4.88$, $p=0.03$), a significant interaction of time and group ($F=6.43$, $p=0.01$) and time by group by postural condition ($F=4.40$, $p=0.012$). This postural condition effect is due to DYN-Firm ($p=0.044$), DYN-Foam ($p=0.049$), and Dark-Firm ($p=0.049$). Healthy military results showed good test-retest and comparable norms to those in civilians (DeMunck thesis 2015, Appendix 8).

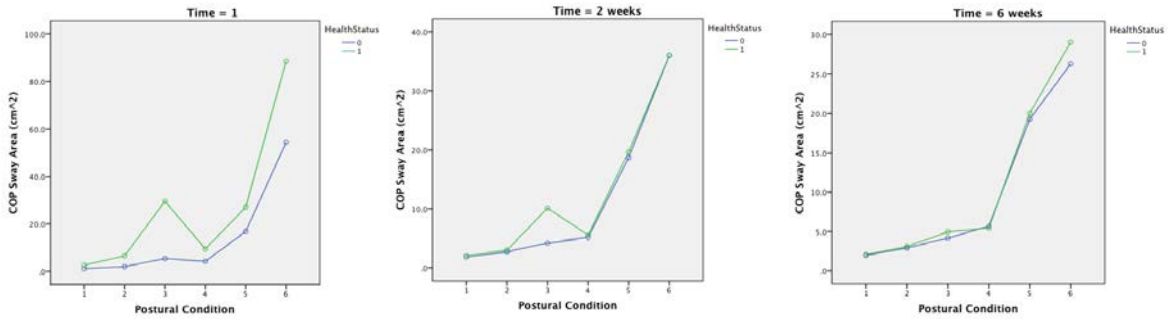

Fig. 4 – Shows change postural control COP sway area across time (Baseline: left, 2-week follow-up: middle, 6-week follow-up: right). The healthy civilian cohort (blue line) performed significantly better than the concussion cohort (green line) at initial test session. Only the Dynamic-Firm condition was different at the 2 week follow-up, and the healthy and concussed groups performed similarly at 6 weeks.

Table 1. Center of Pressure Sway Area (cm^2)

HEALTHY Civilian	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	1.2	2.1	7.0	4.6	19.0	55.9
Std Dev	0.8	1.5	9.8	2.7	10.1	37.3
2-weeks						
Mean	1.8	2.7	4.0	5.1	18.3	34.7
Std Dev	1.7	2.7	4.4	4.2	10.1	23.4
6-weeks						
Mean	1.9	2.9	4.0	5.6	19.3	26.0
Std Dev	2.5	2.6	4.2	4.1	10.1	12.7
HEALTHY Military-NPS	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	1.8	3.2	4.2	4.4	23.5	24.4
Std Dev	0.3	4.0	3.0	0.3	17.3	21.7
1-week						
Mean	3.7	1.8	3.2	4.8	16.2	15.9
Std Dev	0.2	1.4	2.7	0.4	8.5	9.2
HEALTHY Military-CG	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	1.2	1.9	2.8	3.3	12.4	14.2
Std Dev	0.57	1.27	1.83	1.52	7.10	11.48
CONCUSSED	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	1.6	3.3	13.1	5.8	21.5	62.6
Std Dev	2.5	6.6	41.6	8.6	16.1	49.4
2-weeks						
Mean	2.4	3.5	7.2	5.9	19.7	38.1
Std Dev	2.8	3.3	14.5	5.0	11.7	23.9
6-weeks						
Mean	2.1	3.1	4.6	5.7	18.9	27.8
Std Dev	2.6	2.8	5.6	4.6	10.0	16.8

Table 2. Center of Pressure Velocity (cm/s)

HEALTHY	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	2.3	2.5	3.4	2.6	4.9	9.0
Std Dev	1.1	1.2	1.9	1.2	2.3	5.3
2-weeks						
Mean	2.5	2.8	3.2	2.9	5.1	7.2
Std Dev	1.5	1.7	2.2	1.7	3.2	5.3
6-weeks						
Mean	2.4	2.7	3.0	2.9	5.1	6.7
Std Dev	1.2	1.3	1.7	1.8	3.8	6.4
CONCUSSED	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	2.3	2.6	3.6	2.7	4.9	8.9
Std Dev	1.1	1.2	2.4	1.2	2.2	5.2
2-weeks						
Mean	2.4	2.8	3.2	2.9	5.0	7.2
Std Dev	1.4	1.6	2.1	1.7	3.1	5.1
6-weeks						
Mean	2.3	2.5	2.9	2.7	4.9	6.6
Std Dev	1.0	1.2	1.5	1.6	3.7	6.4

Table 3. Root Mean Square Medial-Lateral (cm)

HEALTHY	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	0.26	0.32	0.48	0.44	0.87	1.44
Std Dev	0.24	0.26	0.25	0.23	0.41	0.63
2-weeks						
Mean	0.22	0.25	0.33	0.42	0.70	0.99
Std Dev	0.20	0.21	0.22	0.25	0.29	0.32
6-weeks						
Mean	0.29	0.36	0.43	0.51	0.89	1.03
Std Dev	0.29	0.32	0.29	0.32	0.36	0.38

CONCUSSED	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	0.36	0.43	0.61	0.51	0.97	1.52
Std Dev	0.45	0.34	0.41	0.36	0.45	0.68
2-weeks						
Mean	0.30	0.35	0.47	0.48	0.85	1.11
Std Dev	0.28	0.26	0.35	0.29	0.41	0.37
6-weeks						
Mean	0.32	0.49	0.47	0.55	0.94	1.10
Std Dev	0.27	0.66	0.29	0.36	0.36	0.38

Table 4. Root Mean Square Anterior-Posterior (cm)

HEALTHY	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	0.32	0.39	0.59	0.63	1.02	1.52
Std Dev	0.29	0.29	0.31	1.36	0.31	0.49
2-weeks						
Mean	0.41	0.52	0.55	0.60	1.16	1.29
Std Dev	0.43	0.47	0.39	0.43	0.45	0.42
6-weeks						
Mean	0.37	0.45	0.47	0.56	1.00	1.10
Std Dev	0.39	0.43	0.36	0.35	0.39	0.36
CONCUSSED	FIRM			FOAM		
	Static	Dark	DYN	Static	Dark	DYN
Baseline						
Mean	0.33	0.43	0.65	0.66	1.01	1.52
Std Dev	0.34	0.38	0.48	1.34	0.44	0.61
2-weeks						
Mean	0.40	0.49	0.54	0.58	1.06	1.24
Std Dev	0.42	0.46	0.39	0.41	0.47	0.48
6-weeks						
Mean	0.39	0.50	0.52	0.62	1.04	1.18
Std Dev	0.46	0.62	0.51	0.61	0.66	0.72

Military testing

Session 1 (baseline): 53 total (healthy, i.e. no recent concussion subjects)
Session 2 (1 week follow-up): 15 total (healthy, i.e. no recent concussion subjects)

The Office of Research Protections/Human Research Protection Office (ORP/HRPO) gave approval for secondary analysis of de-identified balance data from the United States Coast Guard (USCG) and Naval Postgraduate School (NPS). Military data includes 53 healthy (USCG: n=38; NPS: n=15). As part of our additional specific aims, we analyzed the USCG balance data in conjunction with subject reported variables regarding lifetime TBI, PTSD and depression in order to determine their effects on postural control (see Table 5).

In the USCG study, a total of 14/36 (39%) participants reported having a previous mTBI. Of those, nine reported having a single concussion incident and five reported more than one incident. Participants with a history of concussion tended to be older ($p < .01$), more educated ($p = .03$), and were deployed more often ($p < .01$) and had greater combat exposure ($p = .05$) than those without a history of concussion. There were no significant differences in total scores on the posttraumatic stress disorder (PTSD) checklist (PCL) with military (PCLM) and nonmilitary (PCLNM) prompts to screen for probable PTSD (pPTSD), and Psychological Health Questionnaire (PHQ-8) for probable depressive disorder (pMDD) (all p's > .05). The total number that met criteria for probable PTSD based on cluster scoring of the PCL-M and PCL-NM was 3/36 (8%); only one probable case was accompanied by a history of mTBI. The total number meeting criteria for probable MDD was 3/35 (9%); only one case was accompanied by a history of mTBI.

Table 5. Demographic and Self-Reported Mental Health Complaints in CG Personnel as a Function of History of mTBI.

	History of mTBI		
	No History (N = 22)	**mTBI History** (N = 14)	***p* value**
Age	25.95 (4.48)	33.57 (7.93)	< .01
Years of Education	12.55 (1.41)	14.00 (2.08)	.03
Deployment History			
Yes	2/21 (10%)	8/14 (57%)	< .01
Combat Exposure			
Yes	2/20 (10%)	5/13 (39%)	.05
PCL-M			
Total Score	23.00 (10.07)	27.50 (16.61)	.33
PCL-NM			
Total Score	25.05 (12.83)	26.14 (7.92)	.78
PHQ-8			
Total Score	3.76 (4.85)	5.00 (5.28)	.48

PCL-M, Posttraumatic Symptom Checklist (Military); PCL-NM, Posttraumatic Symptom Checklist (Non-Military); PHQ-8, Personal Health Questionnaire 8. *Note*. *p*-values correspond to independent samples *t*-tests for continuous values and chi-square tests for categorical values.

In the VETS protocol testing of USCG personnel, data from four participants were unusable for analysis due to system error and lack of self-report inventory. For the

remaining participants (N=32), COP sway area was analyzed w.r.t. Lifetime mTBI. There were no significant between-group or within-group effects (all p's > .05), however, there were trends towards a main effect of Surface (F = 2.98, p = 0.10) and a Surface x Condition x Lifetime mTBI interaction (F = 2.75, p = 0.10). When analyzing COP sway area as a function of number of previous mTBI incidents (0, 1, >1), there were significant main effects of Surface (F = 5.09, p = 0.03) and a Surface x Condition x Number of mTBI Incidents interaction (F = 5.0, p = 0.002). Participants with more than one concussion produced the greatest COP sway area in the dynamic scene on foam surface condition (Fig 5). Those active duty CG personnel with lifetime history of mTBI, but without current complaints such as with persistent post-concussive symptoms (PPCS), did not exhibit neurocognitive deficits. Their ability to maintain balance on a stable surface (eyes open, closed and viewing the dynamic scene) and on foam surface (both eyes open and eyes closed), suggests visuomotor and somatomotor integration are unaffected, however, those reporting multiple past concussions showed deficits in the most demanding balance task on a foam surface while viewing a moving visual scene. This suggests visuo-vestibular integration remains impaired in those previously and repeatedly concussed.

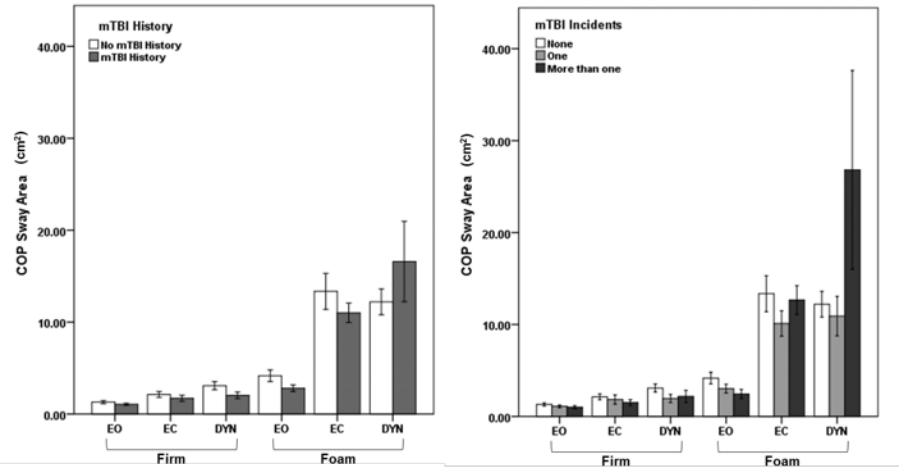

Fig 5. Comparison of VETS COP sway area in CG personnel as a function of mTBI history (left panel) and number of mTBI incidents (right panel). EO, eyes open; EC, eyes closed; DYN, dynamic. Error bars represent ± 1 standard error of the mean.

Balance and oculomotor assessment model

In on-going tests to ensure the VETS protocol validation relative to the best criterion measures, we conducted a series of tests to evaluate the discriminant validity of a battery of vestibular and ocular-motor, and balance assessments on healthy and concussed individuals. These investigations allowed us to develop a new condensed model to assess sensorimotor impairments following a concussion. In the protocol that we conducted, each participant was tested in a concussion assessment protocol that consisted the Neurocom's Sensory Organization Test, Balance Error Scoring System exam, and a series of eight vestibular and ocular-motor assessments.

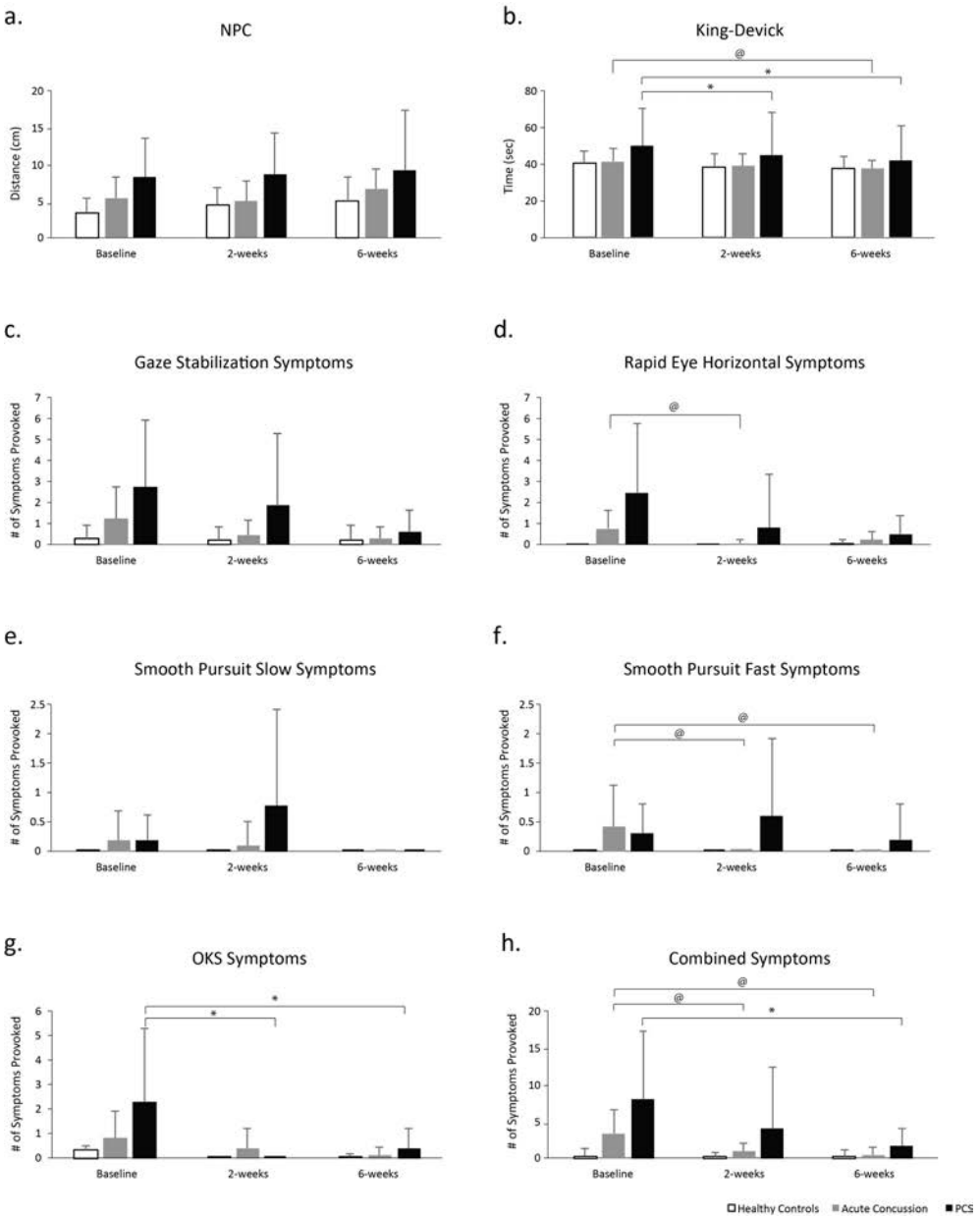

Fig 6. Comparisons across time (baseline, 2-weeks, 6-weeks) for each group healthy (white bars), acutely concussed (grey bars), prolonged PCS (black bars). The healthy group showed no changes across time in any assessment. Near point of convergence (NPC), Gaze stabilization test (GST) and SPS (slow smooth pursuit) showed no change across time. KD (King-Devick Test, total time), REH (rapid eye horizontal), SPF (fast smooth pursuit), OKS (optokinetic stimulation), Combined S/S all showed changes across time.
*Significant differences across time in the PCS group at $p<.05$.
@ Significant differences across time in the Acute group at $p<.05$.

The objectives of these tests were to evaluate several readily available vestibular and oculomotor tests for assessing symptom provocation, tracking recovery across time, and determining how these correlate with the VETS balance assessment. As is the other civilian data collections, three time points were collected (initial, 2-week and 6-week follow-up). We were able to identify three groups within our sample, the acute injury group (n=21) suffered a concussion ≤9 days prior to initial assessment, while the

prolonged post-concussive symptoms (n=10) group suffered a concussion ≥16 days prior to initial assessment. The healthy (n=58) had not experienced a concussion in >6 months. Vestibular and oculomotor assessments were used to measure symptom provocation. Our results showed that provoked symptoms for the Gaze-Stabilization (GST), Rapid Eye Horizontal (REH), Smooth-Pursuit Slow (SPS) and Fast (SPF), and Optokinetic Stimulation (OKS) tests, total combined symptoms scores and near point of convergence (NPC) distance were significantly greater at baseline for acute and prolonged symptoms groups compared to controls. Changes across time showed improvement in both injury groups on the King-Devick test and combined symptom provocation scores. The acute group symptoms improved over time on REH and SPF tests, while the prolonged symptoms group improved in the OKS test (Fig 6). A regression model using REH, OKS, and GST was 90% accurate discriminating healthy versus concussed. From these findings we were able to determine which vestibular and ocular motor tests may increase accuracy of injury recovery and then combine these results with the VETS balance assessments.

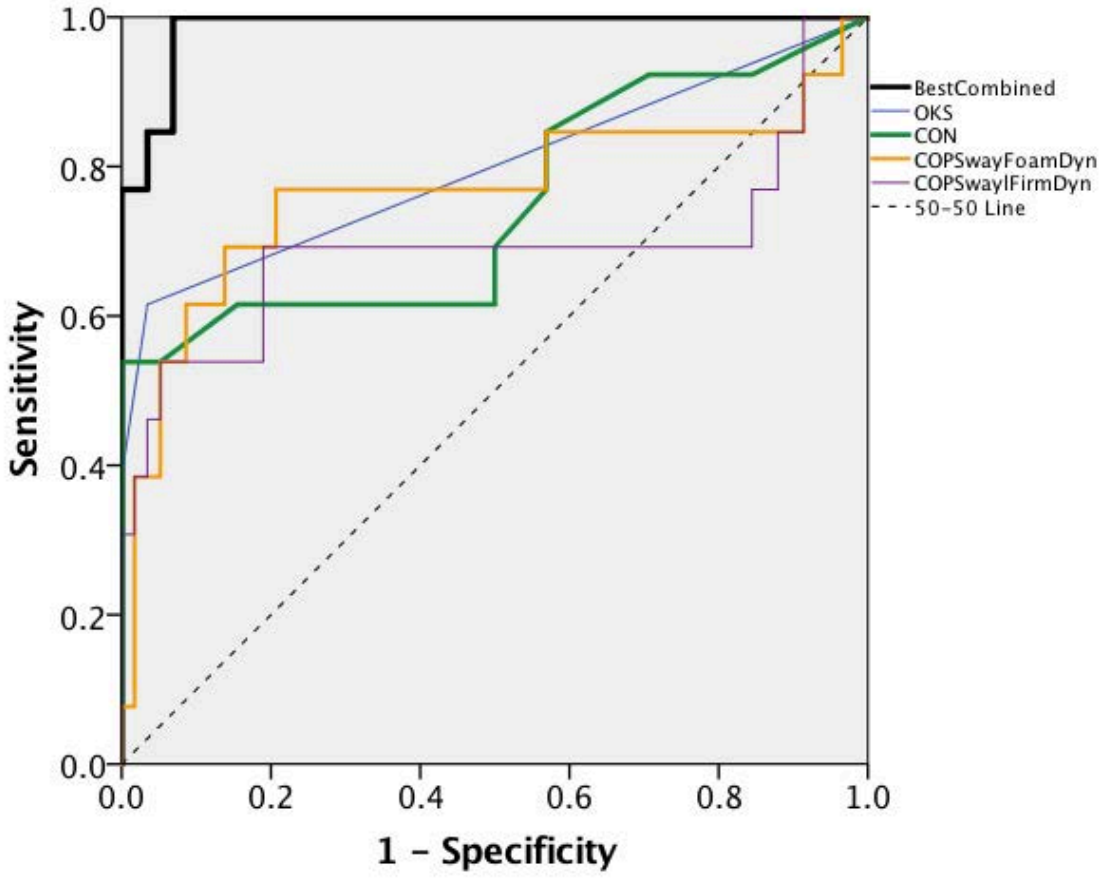

Fig 7. ROC curves from individual visual-vestibular (OKS), oculomotor (convergence - CON), and VETS conditions (Dynamic visual on Firm or Foam surface), and a combined logistic regression model (thick black line), which has an area under the curve of 0.983 (93% specificity and 100% sensitivity).

Of these ten assessments, only the SOT, near point convergence, and the signs and symptoms (s/s) scores collected following optokinetic stimulation, the horizontal eye saccades test, and the gaze stabilization test were significantly correlated with health

status, and were used in further analyses. Multivariate logistic regression for binary outcomes was employed and these beta weights were used to calculate the area under the receiver operating characteristic curve (AUC). The best model supported by our findings suggest that an exam consisting of the four SOT sensory ratios, near point convergence, and the optokinetic stimulation signs and symptoms score are sensitive in discriminating concussed civilian athletes from healthy controls (accuracy = 98.6%, AUC = 0.983). However, an even more parsimonious model consisting of only the optokinetic stimulation and gaze stabilization test s/s scores and near point convergence was found to be a sensitive model for discriminating concussed athletes from healthy controls (accuracy = 94.4%, AUC = 0.951) without the need for expensive equipment (Fig 7). Although more investigation is needed, these findings will be helpful to health professionals potentially providing them with a sensitive and specific battery of simple vestibular and ocular-motor assessments for concussion management. This study can be found in the appendices (McDevitt et al 2016, Cheever et al, *submitted*). The next step in this study is determining whether a model that incorporates VETS with vestibular-oculomotor assessments so that the most economical and accurate objective battery of assessments can be identified.

Results from the USCG study (eye blink studies)

Because very little is known about the interaction stress-related mental health disorders, personality factors, and neurocognitive performance of military individuals serving in the US Coast Guard a study was initiated to investigate these variables and gain greater insight into this understudied military population. The project that was begun before the initiation of this CDMRP contract was proposed to include data collection on over 400 USCG service members. Before the project was put on hold, data from 241 CG personnel (22% female) was collected (see Table 6). The analysis of this data set has been carried out over the last 18 months. The experimental protocol that was completed included a battery of scales: the posttraumatic stress disorder (PTSD) checklist (PCL) with military (PCLM) and nonmilitary (PCLNM) prompts to screen for probable PTSD (pPTSD), and Psychological Health Questionnaire (PHQ-8) for probable depressive disorder (pMDD), the Defense Automated Neurobehavioral Assessment (DANA) battery for assessing neurocognitive performance. The findings showed from a cluster scoring of PCLM and PCLNM that probable PTSD of 6% and 13%, respectively in USCG personnel and an overall rate of 15%. Probable MDD was found to be 15% using aggregate scoring. In hierarchical logistic regression, pPTSD was predicted by combat exposure, behavioral inhibition (BI) temperament (i.e. withdrawal in the face of social and nonsocial challenges) and Type D personality (negative affect combined with social inhibition). Probably MDD was predicted by combat exposure, female sex, and Type D. Probable PTSD was associated with poorer recognition memory, whereas depression was associated with deficits in Go/No-Go (GNG). In multinomial regression, Type D personality predicted pPTSD, pMDD and comorbid pPTSD/pMDD. BI temperament predicted comorbid pPTSD/pMDD, whereas GNG throughput classified pMDD. From this study it was concluded that stress-related mental health symptoms are comparable in CG to larger military agencies and civilian first responders. Diathesis models linking individual vulnerabilities (BI temperament, Type D personality and sex) with traumatic

experiences provide structure to the understanding of stress-related mental health issues in active duty military. A model including personality factors and objective neurocognitive tests identified and distinguished pPTSD from pMDD. (Servatius et al, *in prep* - Appendix 10).

In a sub-group analysis of the USCG data, a learning diathesis model for PTSD was investigated. This model suggests that inherent positive biases in associative learning potentiate avoidance following trauma. The Servatius group recently reported strong associations between BI temperament and distressed (Type D) personality with probable PTSD in CG personnel (Myers et al 2012). They determined whether positive learning biases are apparent in BI and Type D as assessed through eyeblink conditioning using a partial reinforcement schedule. In this subgroup analysis, data from 79 participants in the CG sample (15 females) were recruited from five CG stations. Again the PCLM and non-military PCL-C were used. Eyeblink conditioning was accomplished with a 500-ms pure tone conditioned stimulus (CS) co-terminating with a 100-ms air-puff unconditional stimulus (US), with interpolation of 50% CS-alone trials. The results are consistent with earlier work showing that facilitated acquisition of the eyeblink response was apparent in BI temperament. Facilitation was also apparent in Type D personality, predominately related to the social inhibition component. Both personality dimensions were associated with greater PTSD symptoms. Rates of learning did not independently predict PTSD symptoms. The conclusions of this study show that those expressing social inhibition and behavioral withdrawal display positive learning biases and stronger PTSD symptoms. Negative affectivity was associated with PTSD, but did not contribute to positive biases. These data in active duty military further support personality dimensions of inhibition and withdrawal as vulnerabilities to the development and expression of PTSD (Handy et al, *draft* - Appendix 11). These two studies and one other in preparation will be submitted for publication after USCG approval.

In a subset of the overall sample data for acoustic startle responses (ASRs) were collected for a total of 26 USCG participants in the study. This is a less studied area for mTBI dysfunction. Loud, abrupt sound elicits movement directed away from the location of the presumed source. The ASR depends on stimulus intensity and rise/fall characteristics. The ASR involves cranial nerves, integration within the pons, and motor pathways and extensive modulatory influences in the brainstem, cerebellar, subcortical and cortical structures. The literature concerning the ASR in TBI is limited. In humans, there is a dearth of studies – not one focusing on the ASR itself. Using the ASR and the International Affective Picture Set (IAPS) to assess emotional reactivity in mTBI, one study found baseline ASRs to be decreased in severe TBI, whereas another reported no differences. Each study examined individuals on average 2.5 years after TBI. As to the affective influence on ASR, while one study found ASRs differentially modified in severe TBI, the other did not. In animals, ASRs are consistently and persistently found to be attenuated in moderate and mild injury. Although limited, the literature suggests that, like postural assessments, ASRs may be attenuated in those experiencing mTBI even in the absence of persistent symptoms. This further highlights the difficult dichotomy of signs versus symptoms in concussion assessment.

Table 6.Demographic Characteristics of the USCG Sample

	Overall	Male	Female	Probability (Male vs. Female)
Age	***N* = 241**	***N* = 189**	***N* = 52**	
<25 years	74 (31%)	43 (23%)	31 (60%)	
25-29 years	82 (34%)	66 (35%)	16 (31%)	$\chi^2(2) = 30.63$, $p < .001$
>29 years	85 (35%)	80 (42%)	5 (9%)	
Ethnicity	***N* = 241**	***N* = 189**	***N* = 52**	
White/Non-Hispanic	176 (73%)	140 (74%)	36 (69%)	
Black/Non-Hispanic	8 (3%)	7 (4%)	1 (2%)	$\chi^2(3) = 1.55$, $p = .671$
Hispanic	35 (15%)	25 (13%)	10 (19%)	
Other	22 (9%)	17 (9%)	5 (10%)	
Education	***N* = 241**	***N* = 189**	***N* = 52**	
Some college or less	197 (82%)	157 (83%)	40 (77%)	$\chi^2(1) = 1.03$, $p = .310$
Bachelor's or higher	44 (18%)	32 (17%)	12 (23%)	
Lifetime Hx of Concussion	***N* = 241**	***N* = 189**	***N* = 52**	
Yes	117 (49%)	105 (56%)	12 (23%)	$\chi^2(1) = 17.22$, $p < .001$
Rank	***N* = 236**	***N* = 185**	***N* = 51**	
Cadet	7 (3%)	3 (2%)	4 (8%)	
Junior Enlisted (E1-E4)	119 (50%)	78 (42%)	41 (80%)	
NCO (E5-E6)	91 (39%)	86 (46%)	5 (10%)	$\chi^2(4) = 34.29$, $p < .001$
Senior NCO (E7-E9)	12 (5%)	12 (6%)	0	
Officer	7 (3%)	6 (3%)	1 (2%)	
Deployment	***N* = 233**	***N* = 184**	***N* = 49**	
Previously Deployed	104 (45%)	94 (51%)	10 (20%)	$\chi^2(1) = 0.61$, $p = .437$
Combat Exposure	***N* = 232**	***N* = 181**	***N* = 51**	
Yes	20 (9%)	19 (11%)	1 (2%)	$\chi^2(1) = 3.68$, $p = .055$
Type D	***N* = 240**	***N* = 188**	***N* = 52**	
Type D	76 (31%)	58 (31%)	18 (35%)	$\chi^2(1) = 0.27$, $p = .606$
BI	***N* = 241**	***N* = 189**	***N* = 52**	
Inhibited	89 (37%)	70 (37%)	19 (37%)	$\chi^2(1) = 0.01$, $p = .947$

ASR data were collected for a total of 26 participants in the USCG study. Of these, three participants were excluded from analysis due to self-reported ringing in the ears. There was an overall main effect of Stimulus Intensity when assessing the probability of an ASR ($F = 3.75$, $p = .03$), however, sensitivity was not affected by Lifetime mTBI ($F = 2.71$, $p = .12$), nor was Lifetime mTBI x Stimulus Intensity interaction significant ($F < 1$, n.s.). In contrast, Lifetime mTBI was associated with suppressed ASR magnitude ($F = 5.57$, $p = .03$); neither the main effect of Stimulus Intensity ($F < 1$, n.s.) nor Lifetime mTBI x Stimulus Intensity interaction were significant for ASR magnitude ($F < 1$, n.s.) (Fig 8). Neither ASR sensitivity nor ASR magnitude differed as a function of Number of mTBI Incidents (Fig 9). Only the main effect of Stimulus Intensity was significant for ASR sensitivity, ($F = 3.53$, $p = .04$). These data are consistent with the overall sample from the larger study (N =183). There are few studies examining ASRs in humans previously concussed. These data suggest that ASRs warrant further study and may provide a sensitive biomarker for mTBI, even after symptoms have disappeared.

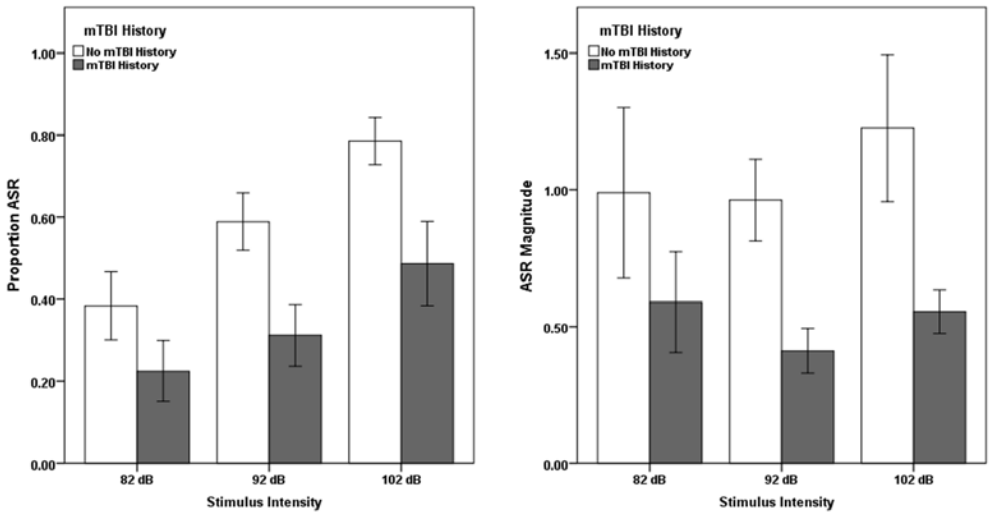

Fig 8. Sensitivity (left panel) and magnitude (right panel) of ASR as a function of mTBI history. dB, decibel. Error bars represent ± 1 standard error of the mean.

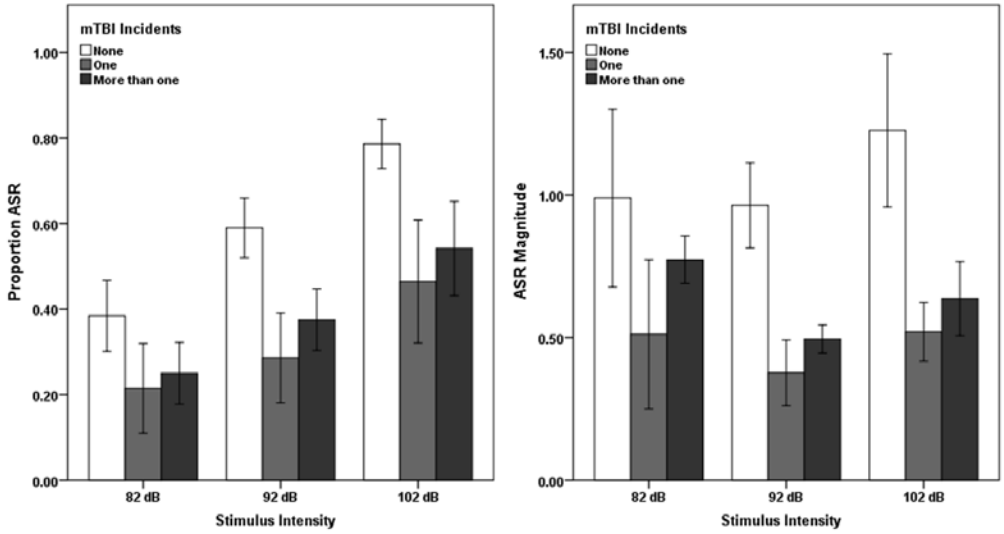

Fig 9. Sensitivity (left panel) and magnitude (right panel) of ASR as a function of number of mTBI incidents. dB, decibel. Error bars represent ± 1 standard error of the mean.

Future Progress

We now have a signed MOU with NHCL. We are currently working out the details of data collection at Camp Lejeune for VETS validation on mTBI and PTSD cohorts. We are working directly with the Director of Intrepid Spirit Concussion Recovery Center, CAPT Thomas M. Johnson, MD (USN Neurologist), who will serve as local PI for new grant proposals, which were invited as full proposals to the latest CDMRP BAA. Data will be collected from patients in the chronic phase of recovery. Currently, Dr. Alex Ortega, who is part of SMBI team led by Dr. Servatius is stationed down at Camp Lejeune, awaiting final IRB approvals so that arm of the project that will involve PTSD data collection can commence.

We have begun collecting data on veterans with PTSD at the Syracuse VAMC, which includes VETS postural testing, oculomotor testing, eye-blink conditioning, and neurocognitive assessments. These tests are part of a new line of research, which investigates the cerebellar effects of TBI, PTSD, and/or depression on the health of military veterans.

4. IMPACT

Our findings using this novel VR-based posturography device suggest that visual-vestibular processing deficits are present in not only subacutely following mild traumatic brain injury, but are also evidence in active duty and veterans who report a lifetime history of mTBI. The combination of specific postural tasks designed to assess the well-calibrated integration of visual and vestibular inputs together with specific visuomotor tests that assess spatial and self-motion perception were found to be the most sensitive tests for discriminating health status following concussion. The comprehensive evaluation of the signs and symptoms allows us to infer which neural processes may be damaged by the injury. It should be noted that assessments largely based on patient reports of symptom provocation rely on the accuracy and integrity of subjective report. Therefore, ensuring subjective measures are supplemented by objective measures such as the VETS device we designed ensures higher fidelity in concussion assessment. Our findings serve to focus attention in on using sensitive tools for assessing symptoms, especially chronic unremitting signs and symptoms, which can help clinical decision-making and guide treatment during the service member's recovery process and will decrease the likelihood that they will return to pre-injury capability levels.

The secondary aims of this project, which included the USCG study, provided greater insight into this understudied military population with regards to the interaction of stress-related mental health disorders, personality factors, and neurocognitive performance in this population. These data further support personality dimensions of inhibition and withdrawal as vulnerabilities to the development and expression of PTSD in active duty military. This will help target rehabilitation of injured service members to accrurately address the underlying etiologies.

5. CHANGES AND PROBLEMS

a. A second separate set of aims was added to the existing contract (W81XWH-13-C-0189) for the purposes of supporting a project that started prior to 2013 which was not part of the original CDMRP project. This on-going project was led by Dr. Richard Servatius and CAPT Jack Tsao USN (ret) and was carried out at USCG stations across the country, with a primary goal of investigating the interaction of PTSD with TBI by focusing on neuromotor and neurobehavioral assessments and epigenetic predictors. The addition of funds in year 2 to the existing CDMRP contract was used to support analysis and preparation of the findings for the USCG project. It was funded by sources other than CDMRP, so data collection had started before the CDMRP contract began. However, because CDMRP will, in part, be funding data analysis, interpretation, publication, a data usage agreement (DUA) to get access to the de-identified Coast Guard data was set up between Temple University, Syracuse VA, and SMBI. The project that was initiated before this CDMRP contract had intended to collectover 400 USCG service members. Data from 241 CG personnel was collected before that project was put on hold by stakeholders outside of this contract and although the US Coast Guard study's data collection was suspended after 2/3 of the data was collected, four reports have been prepared for dissemination. The analysis of the USCG study data is, however, still underway because a s/w error was identified and a workaround was implemented in the protocol instructions that affected data processing. This required an additional workload on the subcontractors for data analysis, however, their funds were depleted and a request to add funds to their subcontract was not approved. Many of these data analyses have been included as preliminary data for our recently submitted applications to the CDMRP.
b. An existing IRB at Naval Hospital Camp Lejeune (NHCL) that Dr. Servatius had already gotten approved was modified to include balance assessment. This IRB expired while awaiting an MOU to be signed off by NHCL command staff. That MOU was finally signed-off in the last month of this contract (i.e. September 2016). In the mean time NHCL has begun developing its own independent IRB which is undergoing review and will become active this year. Our IRB for the Intrepid Spirit Concussion Recovery Center, Camp Lejeune, NC, which falls under the umbrella of NHCL has been re-submitted to the Research Quality Council. Once this is approved project that uses VETS to further investigate mTBI and PTSD will commence.

6. REPORTABLE OUTCOMES:

Papers and Presentations

Papers

Wright WG, McDevitt J, Appiah-Kubi K (2015) A portable virtual reality balance device to assess mild traumatic brain injury symptoms: A pilot validation study. *IEEE Proc ICVR2015*, pp 72-79. doi: 10.1109/ICVR.2015.7358591. (See Appendix 3)

Haran FJ, Slaboda JC, King LA, Wright WG, Houlihan D, Norris JN (2016). Sensitivity of the Balance Error Scoring System and the Sensory Organization Test in the Combat Environment. *Journal of Neurotrauma*. 33(7):705-11. PubMed PMID: 26560740. (See Appendix 7)

Wright WG, McDevitt JK, Tierney R, Haran FJ, Appiah-Kubi KO, Dumont A (2016). Assessing subacute mild traumatic brain injury with a portable virtual reality balance device. *Disability and Rehabilitation*. [ePub ahead of print] (See Appendix 4)

McDevitt J, Appiah-Kubi K, Tierney R, Wright WG (2016) Vestibular and Oculomotor Assessments May Increase Accuracy of Subacute Concussion Assessment. *Int J Sports Med*. 37:738-747. doi: http://dx.doi.org/10.1055/s-0042-100470 (See Appendix 5)

Rhea CK, Kuznetsov NA, Bailie JM, Yanagi MA, Long B, Haran FJ, Ross SE, Wright WG, Robins RK, Jakiela JT, Sargent PD, Duckworth JL (*in press*). Development of a portable tool for screening neuromotor sequelae from repetitive low-level blast exposure. *Journal of Military Medicine*.

Wright WG, Tierney R, McDevitt JK (*in press*) Visual-vestibular processing deficits in subacute mild traumatic brain injury. *Journal of Vestibular Research*. (See Appendix 6)

Cheever K, McDevitt JK, Tierney R, Wright WG. Effects of concussion recovery phase on symptom provocation using vestibulo-ocular motor assessments (*submitted*). (See Appendix 9)

Wright WG, Handy JD, Avcu P, Ortiz A, Haran FJ, Doria MJ, Servatius RJ (*submitted*) Healthy Active Duty Military with Lifetime Experience of Mild Traumatic Brain Injury Exhibit Subtle Deficits in Sensory Reactivity and Sensory Integration during Static Balance. *Journal of Military Medicine*.

Servatius RJ, Handy JD, Doria MJ, Myers CE, Marx CE, Lipsky R, Lathan CE, Ko N, Avcu P, Wright WG, Tsao JW (*submitted*). Stress-Related Mental Health Symptoms and Neurocognitive Function in Active Duty Coast Guard Personnel. (See Appendix 10)

Handy JD, Avcu P, Ortiz A, Doria MJ, Servatius RJ. Facilitated Eyeblink Conditioning and Heightened Posttraumatic Symptoms in Active Duty Military Expressing Social Inhibition. *Manuscript ready for submission*. (See Appendix 11)

Handy JD, Doria M, Servatius RJ. Cross-sectional Assessment of Stress-Related Mental Health Symptoms and Neurocognitive Function in Active Duty Coast Guard Personnel. *Manuscript in prep.*

Military technical report for USCG: "Cognitive Assessment in Coast Guard Personnel: Neuroendocrine, Genetic, and Epigenetic Correlates."

Invited podium talks

UNC-Greensboro, Motor Behavior Research Network, April 16, 2015
Title: "Validating an affordable and portable Virtual Reality balance device for assessing mTBI symptoms and recovery". Presented by Wright WG

International Conference for Virtual Rehabilitation (ICVR), Valencia, Spain
Conference dates June 9-12, 2015
Title: "A portable virtual reality balance device to assess mild traumatic brain injury symptoms: A pilot validation study". Presented by Wright WG

Temple University Concussion Summit: Current Trends in Concussion Assessment & Risk Factors, Philadelphia, PA, 20 Jun 2015
Title: "A portable virtual reality balance device to assess mTBI symptoms: A pilot validation study"
Prepared by Wright WG, McDevitt JK, Appiah KO, Dumont A. Presented by McDevitt JK.

International Society of Gait and Posture Research (ISPGR), Sevilla, Spain.
Conference dates June 28-Jul 2, 2015
Title: "Using commercial technology to create a portable VR balance device to assess mTBI symptoms"
Presented by Wright WG

McDevitt JM, Appiah-Kubi K, Tierney RT, Wright WG. "Vestibular and Oculomotor Assessments May Increase Accuracy of Subacute Concussion Assessment", *NATA*, Baltimore, MD, June 2016.

Wright WG, McDevitt J, Tierney R, Appiah-Kubi K. "Using a novel postural assessment device to detect balance deficits following mild traumatic brain injury". *NASPSPA*, Montreal, Canada, June 2016.

Wright WG, Haran FJ, Tierney R, McDevitt J. "Assessing subacute mild traumatic brain injury with a portable field-deployable virtual reality balance device", MHSRS 2016, Orlando, FL. August 2016.

Poster presentations

Dumont A, Appiah-Kubi K, Dumont M, Wright WG, "Feasibility of Affordable Custom-Designed Device with Immersive Virtual Environment for Postural Assessment". *Society for Neuroscience*, Washington, DC. Nov 2014. Presented by W. Geoffrey Wright.

Dumont A, Appiah-Kubi K, Dumont M, Wright WG. Title: "Feasibility of Affordable Custom-Designed Device with Immersive Virtual Environment for Postural Assessment". *College of Public Health Research Day*, Temple University. April 2015. Presented by Alex Dumont. This poster was awarded the "Meritorious Poster Award".

Appiah-Kubi KO, McDevitt J, Wright WG. Title: "A portable virtual reality balance device to assess mTBI symptoms: a pilot validation study". *College of Public Health Research Day*, Temple University. April 2015. Presented by Kwadwo Appiah-Kubi.

Wright WG, McDevitt J, Tierney R, Haran FJ, Appiah-Kubi KO. Title: "A novel use of commercially available technology to assess balance impairment in mild traumatic brain injury". *Society for Neuroscience*, Chicago, IL. Oct 2015. Presented by W. Geoffrey Wright.

Appiah-Kubi K, Wright WG, "Effects of Vestibular Training on Postural Control in Healthy Adults", *College of Public Health Research Day*, Temple University. April 2016. Presented by Kwadwo Appiah-Kubi.

Handy JD, Avcu P, Ko N, Ortiz A, Liberzon I, Marx C, Doria M, Servatius RJ. Facilitated Acquisition of the Conditioned Eyeblink Response in Active Duty Coast Guard Personnel Expressing Type D Personality. *Society of Biological Psychiatry Abstract.* Atlanta, Georgia, May 2016.

Rhea CK, Kuznetsov NA, Bailie JM, Yanagi MA, Long B, Haran FJ, Ross SE, Wright WG, Robins RK, Jakiela JT, Sargent PD, Duckworth JL. "Concussion history influences neuromotor performance after exposure to repetitive low-level blast exposure". *American Society of Biomechanics*, Raleigh, NC, August 2016.

Wright WG, Tierney RT, McDevitt JK. "Visual-vestibular processing deficits in subacute mild traumatic brain injury". *Society for Neuroscience*, San Diego, CA. Nov 2016. *Accepted for presentation*.

Career progression of team members

The PI (WGW) was promoted to Associate Professor, in part, due to the accomplishments associated with this project. Dr. Wright research on military brain injury led to an appointment (WOC) at the Syracuse VA and he was invited to be a member of Stress and Motivated Behavior Institute (SMBI), an Institute co-sponsored by

the Armament Research Development Engineering Center (ARDEC). He was also invited to be an independent reviewer for the Upstate Medical University Research Conflict of Interest (RCOI) Committee.

Dr. Ryan Tierney was selected to lead an arm of the NCAA-DoD CARE Consortium and received funding from Army Research Lab with Dr. Wright (Co-I).

LT Jay Haran was promoted to O-4 USN, in part, due to involvement of this project.

The project coordinator, Dr. Jane McDevitt became a tenure-track assistant professorship appointment at East Stroudsburg University. She continues to be part of the team, helping with FITBIR and collecting data on individuals with concussion.

The lead computer programmer, Maxim Dumont, was hired by Comcast as a full-time computer programming. He continues to consult on the project pro-bono.

In collaboration with Temple team members, the PI and new programmer (Greg Teodoro), the latest version of VETS was released this quarter.

Alex Dumont – was accepted and matriculated into the PhD Program in Bioengineering at Temple University after completing his M.S. with support from this contract.

Kelly Cheever, MS, ATC has been appointed the lead study coordinator of the TUCARES project in support of the NCAA-DoD CARES Consortium.

<u>Funding applied for based on work supported by this award</u>

PI: Wright WG, DoD Congressionally Directed Medical Research Program (CDMRP). Title: "Using a Novel, Portable Virtual Reality-Based System to Assess and Rehabilitate Individuals with mTBI with and without PTSD"
Passed Step-1 review. Full proposal invited for Nov 2016 deadline.

Co-I: Wright WG, PI: Servatius R: DoD Congressionally Directed Medical Research Program (CDMRP). Title: "Tracking the effects of TBI on cerebellar dysfunction in a military population."
Passed Step-1 review. Full proposal invited for Nov 2016 deadline.

Co-I: Wright WG, PI: Marx C. DoD Congressionally Directed Medical Research Program (CDMRP). Title: "Accelerating return to duty and ameliorating pain symptoms following complex TBI: Investigation of neurosteroids and therapeutic interventions."
Passed Step-1 review. Full proposal invited for Nov 2016 deadline.

Site-PI: Tierney R. NCAA-DoD CARE Consortium longitudinal clinical assessment study. Funded.

Co-PI: Tierney, Co-I: Wright WG. Army Research Laboratories. Concussion research grant. Funded.

Site-PI: Wright WG, PI: Rhea C, DoD Defense Health Program. Title: "TBI Assessment of Readiness Using a Gait Evaluation Test (TARGET): Development of a Portable mTBI Screening Device". Funded.

Site-PI: Wright WG, PI: Rhea C, DoD Defense Health Program. Title: "Rehabilitation Engagement Visualized in Virtual Environments (REVIVE): Enhancing gait rehabilitation after lower-limb amputation". Passed Step-1. Not Funded.

Co-I: Wright WG, PI: Servatius R, DoD Congressionally Directed Medical Research Program (CDMRP). Title: "TBI Endpoints Development (TED) team". Passed Step-1. Not Funded.

7. PROJECT STAFF & OTHER COLLABORATING ORGANIZATIONS

W. Geoffrey Wright, PhD	Role: PI Nearest person months worked in YR3: 5 Program oversight of all aspects of project, all personnel, and liaison for all subcontracts
Ryan Tierney, PhD, ATC	Role: Co-I Nearest person months worked in YR3: 1 Coordination of concussion recruitment, sports concussion consultation
Maxim Dumont	Role: Lead Computer programmer (2013-2015) Nearest person months worked in YR3: 1 Design and architecture of all s/w for VETS user interface
Greg Teodoro, MS	Role: Lead Computer programmer (2016) Nearest person months worked in YR3: 3 Update and optimize of all s/w for new releases of VETS user interface
Jane McDevitt, PhD	Role: Lab Coordinator Nearest person months worked in YR3: 0.5 Concussion Specialist; Subject recruitment; data collection; data analysis
Alex Dumont	Role: Graduate Research Assistant Nearest person months worked in YR3: 7 Electronics maintenance; computer programming; data analysis; presentation preparation
Kwadwo Appiah-Kubi, PT	Role: Graduate Research Assistant Nearest person months worked in YR3: 12 Data collection; data analysis; presentation preparation
Kelly Cheever MS, ATC	Role: Graduate Research Assistant Nearest person months worked in YR3: 8 Data collection; data analysis; presentation preparation
LT Jay Haran, PhD	Role: Co-PI Nearest person months worked in YR3: 0.5 Oversight of military aspects of project, military liaison for subcontracts
Richard Servatius, PhD	Role: Subcontractor (Rutgers University and Syracuse VA) Nearest person months worked in YR3: 4 Oversight of USCG and NHCL arms of the PTSD+mTBI project

Contract expenditures to date – Final numbers will be processed within the federal 90 day close-out window (as applicable):

This Qtr/Cumulative	**This Qtr/Cumulative**
Personnel:	Travel:
Fringe Benefits:	Equipment:

Supplies: Other:
Subcontracts: Tuition:

This Qtr/Cumulative
Subtotal:
Indirect Costs:
Fee:
Total:

8. CONCLUSION

In our third and final year we have succeeded in accomplishing our Major tasks aimed at testing the sensitivity and specificity of a novel, field-deployable postural assessment protocol relative to existing criterion-measures. We have designed and implemented this custom-designed portable virtual reality-based postural assessment device on healthy military and civilian cohorts and concussed civilians. We have established a database of healthy normative levels for the VETS protocol (n=92), determined reliability across 3 test sessions and used these norms to compare with our concussion sample (n=34). We found the VETS protocol to be as sensitive and specific as the "gold standard" Neurocom SOT. The great benefit of this device is that it costs 1/100th the price (i.e. <$1000) of the "gold standard" SOT ($70,000-$150,000). Moreover, our findings show that the VETS protocol is sensitive to long lasting unremitting symptoms that the BESS cannot detect. Having established the reliability and validity of this device for assessing concussion, future steps will include testing this on a military cohort with unremitting symptoms at Naval Hospital Camp Lejeune using our newly established MOU. We will also assess the specificity of the VETS protocol for dissociating balance and dizziness symptoms that have a psychogenic etiology possibly related to PTSD from the balance and dizziness symptoms that may be visual-vestibular in origin due to TBI-related etiology. Since these two pathologies frequently co-occur in military service members, a deeper understanding of how they overlap and differ is critical to the health of the warfighter.

Additional References

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Langlois JA, Rutland-Brown W, Wald MM. The epidemiology and impact of traumatic brain injury: a brief overview. J Head Trauma Rehabil 2006;21:375–378.

Mucha A, Collins MW, Elbin RJ, Furman JM, Troutman-Enseki C, DeWolf RM, Marchetti G, Kontos AP. A Brief Vestibular/Ocular Motor Screening (VOMS) Assessment to Evaluate Concussions: Preliminary Findings. Am J Sports Med. 2014 Oct;42(10):2479-86.

Myers CE, Vanmeenen KM, McAuley JD, Beck KD, Pang KC, Servatius RJ. Behaviorally inhibited temperament is associated with severity of post-traumatic stress disorder symptoms and faster eyeblink conditioning in veterans. Stress. 2012;15:31-44.

APPENDICES:

1. VETS User Manual
2. VETS Program Design Architecture
3. Wright et al 2015, Proceedings of ICVR2015
4. Wright et al 2016, Disability and Rehabilitation
5. McDevitt et al 2016, International Journal of Sports Medicine
6. Wright, Tierney, McDevitt (accepted) Journal of Vestibular Research
7. Haran et al (2016) Journal of Neurotrauma
8. DeMunck thesis – Naval Postgraduate School
9. Cheever et al (submitted)
10. Servatius et al (submitted)
11. Handy et al (draft ready for submission)

Appendix 1

VETS USER MANUAL

1 Introduction

Hello and welcome to the VETS user manual. If you are wondering what the letters in VETS stand for, they are Virtual Environment TBI (traumatic brain injury) Screening. The objective of this project was to design a piece of reliable software that could capture center of pressure data from a Wii Balance Board (WBB) and give the raw data to the user to use in different ways. For this purpose, we've made the software as generic and simple as possible. All it consists of is 4 visual tabs, in order: LiveMode, Settings, Results and Play. There is a certain methodology in place here for why these tabs are placed so. We could have combined Settings and Play tabs, but purposefully did not.

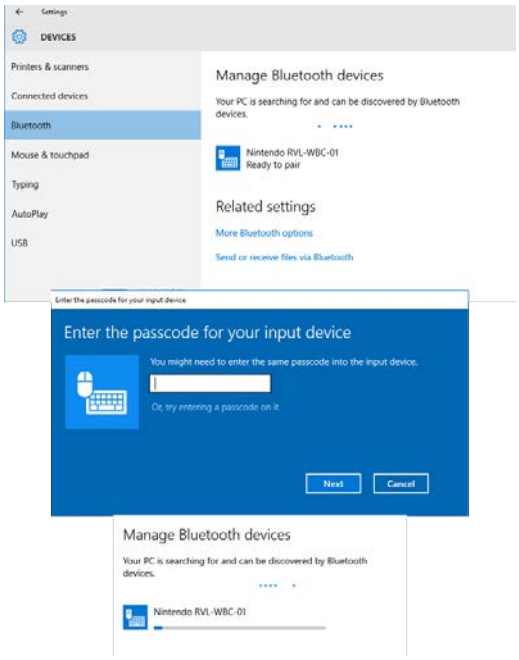
2 LiveMode

Live Mode was designed to show immediate information about the particular balance board connected via Bluetooth. There is no recording option on this page. If the balance board is not connected, the central part of the plot surface will display "no data to plot". In parallel, the display at the bottom right corner will say "Cannot connect to balance board". The Top Left, Top Right, Bottom Left, Bottom Right, Total Weight and Battery Status will all display .0% or .0kg in the case that no balance board is successfully connected. The user may proceed with data collection even if no balance board is connected, but the results will display zeroes or all fields and the outputted XML files for that trial will be empty.

The user can connect to a WBB in search mode by clicking the "Connect To WBB" on the Live Mode screen, or manually connecting to the device via the Bluetooth menu on the computer. If the user utilizes the Bluetooth stack provided by MICROSOFT, move the mouse to the right bottom corner of the screen, there should be a Bluetooth logo. Click on the Bluetooth logo and several options should become available to the user. By clicking on the "Add a Bluetooth Device", the user will be redirected to the Bluetooth panel in "discovery mode". Alternatively, the user can go to control panel→devices→bluetooth which will reach the same page. The WBB should not be visible on this page yet. Clicking the red button on the inside of the battery case on the WBB will make the device discoverable and should be recognized as "Input Device" or "Nintendo RVL-WBC-01" on the computer. The last name is hard-coded into the WBB. By clicking on the "Nintendo RVL-WBC-01", a button appears in the bottom right corner of the item named "Pair". This button will last approximately 15 seconds after the user has pressed the red button. The user may hold in the red button to extend the time the device is discoverable, otherwise, the user will have approximately 15 seconds to click pair. Once pair is clicked, a pop-up menu will appear asking for a passcode. This is not necessary and the user may click "Next" *without* entering a passcode. In the case that errors occur at any point of the process, the user may try different general solutions. These are to restart the procedure from the start or restart the computer.

Alternatively, the user may choose to connect to the WBB by using the "Connect to WBB" on the LiveMode of the application. In this case, the application will check if the is connected to the machine,

and if it is not, will go into discoverable mode. The user should concurrently press the red button on the WBB. Restarting the application manually should reveal that the WBB has successfully connected.



The read out panel has several functions available to it. These are present in the Read Out heading tile. The user can set this header to auto-hide, hide, or docked mode, which depends on whether or not the user wants the subject to see that information.

Once the WBB has been connected via Bluetooth, the blue light on the front of the device should be a constant blue. The Live Mode Visual Readout should now display the center of pressure in live time at a refresh rate of 100 ms. The top left, top right, bottom left, bottom right, total weight, and battery status should all display results at this point. Interestingly enough, the WBB makes a pretty decent scale. The tab at the bottom right should at this point be green, orange or red depending on the battery status of the WBB. If the tab is green, the batteries are fully charge, if the tab is orange or red, the batteries are depleted to various extents and the simulation may not be as successful.

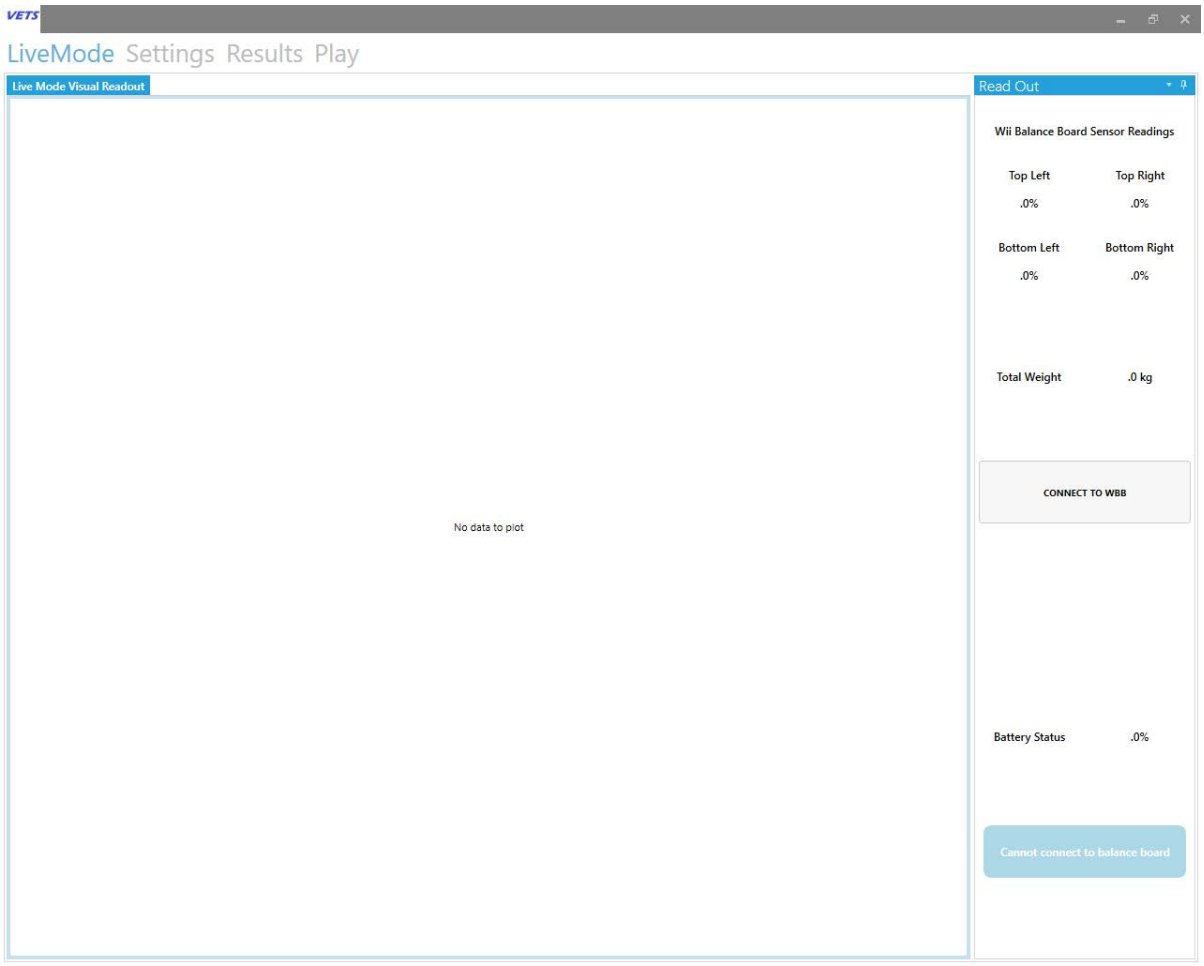


*Figure 1. Appearance of the LiveMode page assuming WBB is not yet paired to the computer. There are several indications that the WBB is not connected at this point, such as the message at the middle of the plotting domain, and the message enclosed in a blue field at the bottom right. The fields also all read 0, is a strong indicator that the WBB is **not** connected. In the un-paired mode, no new balance data can be collected, but the functionality of the rest of the program will be unaffected. If the user does run a trial while the WBB is un-paired, the collected data in file will show all 0's.*

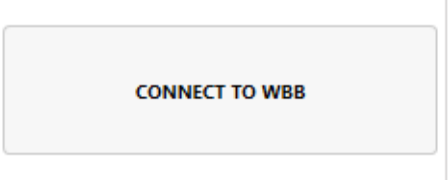


Figure 2 The user can pair with the WBB by simply using the button on the middle right part of the LiveMode screen,. Waiting a few seconds and restarting the program. Alternatively, the user can go through the add a device or the Bluetooth logo typically at the bottom right of the monitor. Once at the Bluetooth page, by pressing the red button on the WBB, the WBB will appear on the selection screen. By clicking pair, a blue screen will appear for a passcode. Leave this part blank ad click next, and the WBB will configure itself.

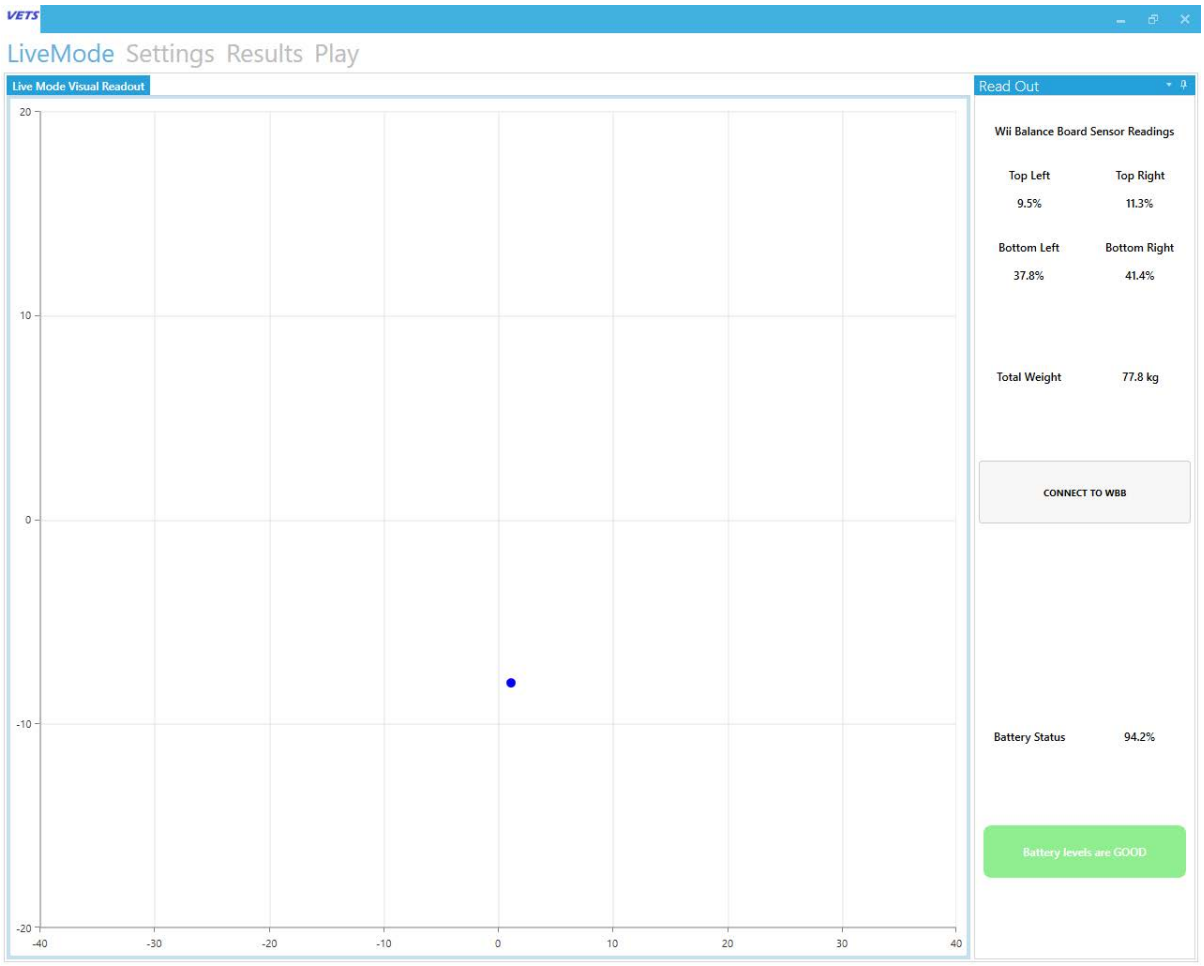
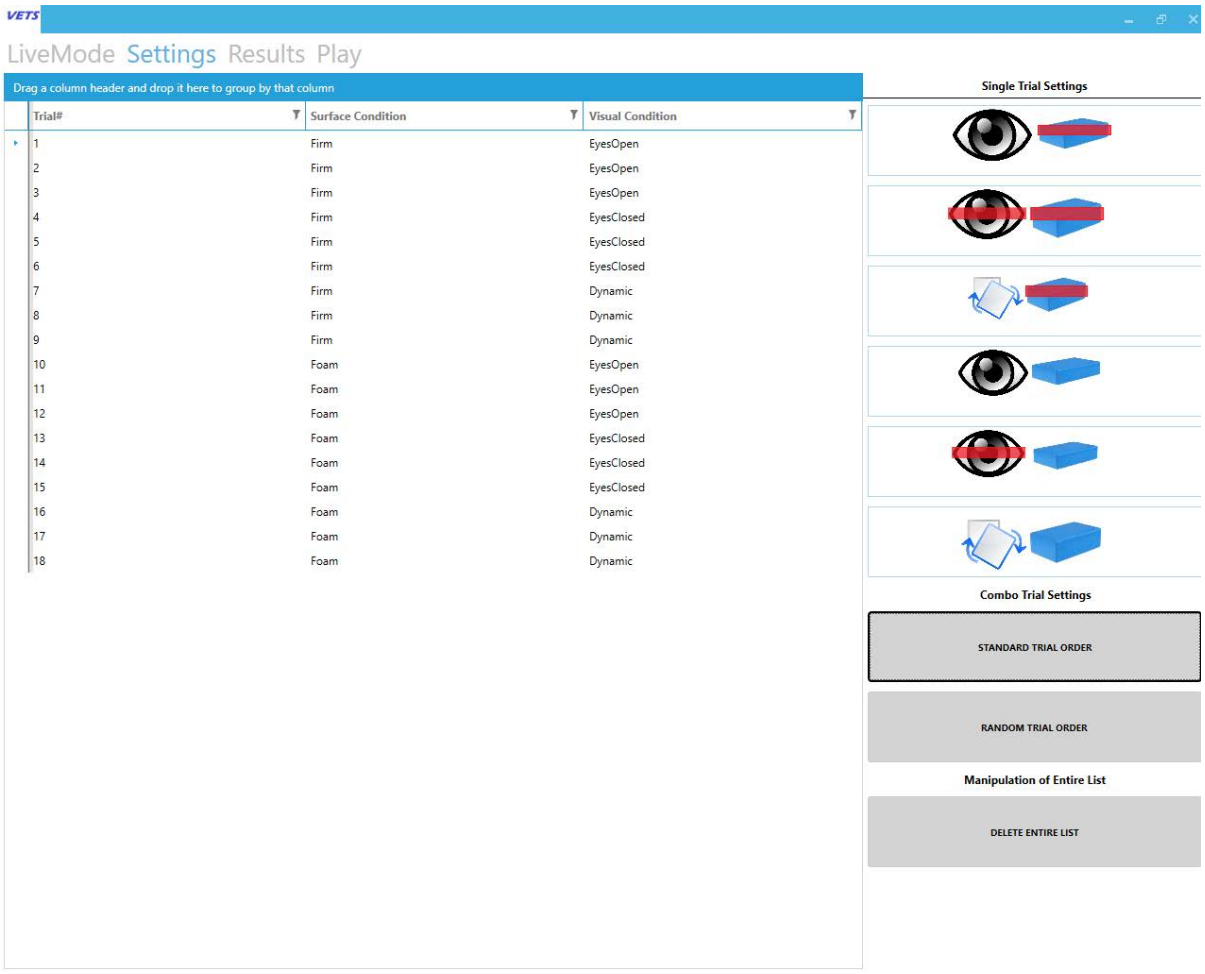


Figure 3. As seen above is a fully functioning VETS program that has successfully been paired to a WBB. The plotting domain now reveals a dot that refreshes every 100 ms, representing the actual sensed center of pressure on the plate in cm. The battery status has been adapted to give the user some sense of how worn the battery is, but the WBB is often inaccurate about its battery status. Once a user has paired with a Wii Balance, he/she should have to repeat the connection setup only once and the WBB should stay connected.

3 Settings

The settings tab is shown below:



The image used is located in ~\Documents\Vets\Image and can be replaced with any image as long as it is the unique image in that directory. Having more than one image will force VETS to choose the latest added image as the display image for the VETS program. Once the image has been specified, or the default image has been kept, the user may specify his/her trials. For the moment, there are six different conditions preset in the screen with visual cues indicating what they are.

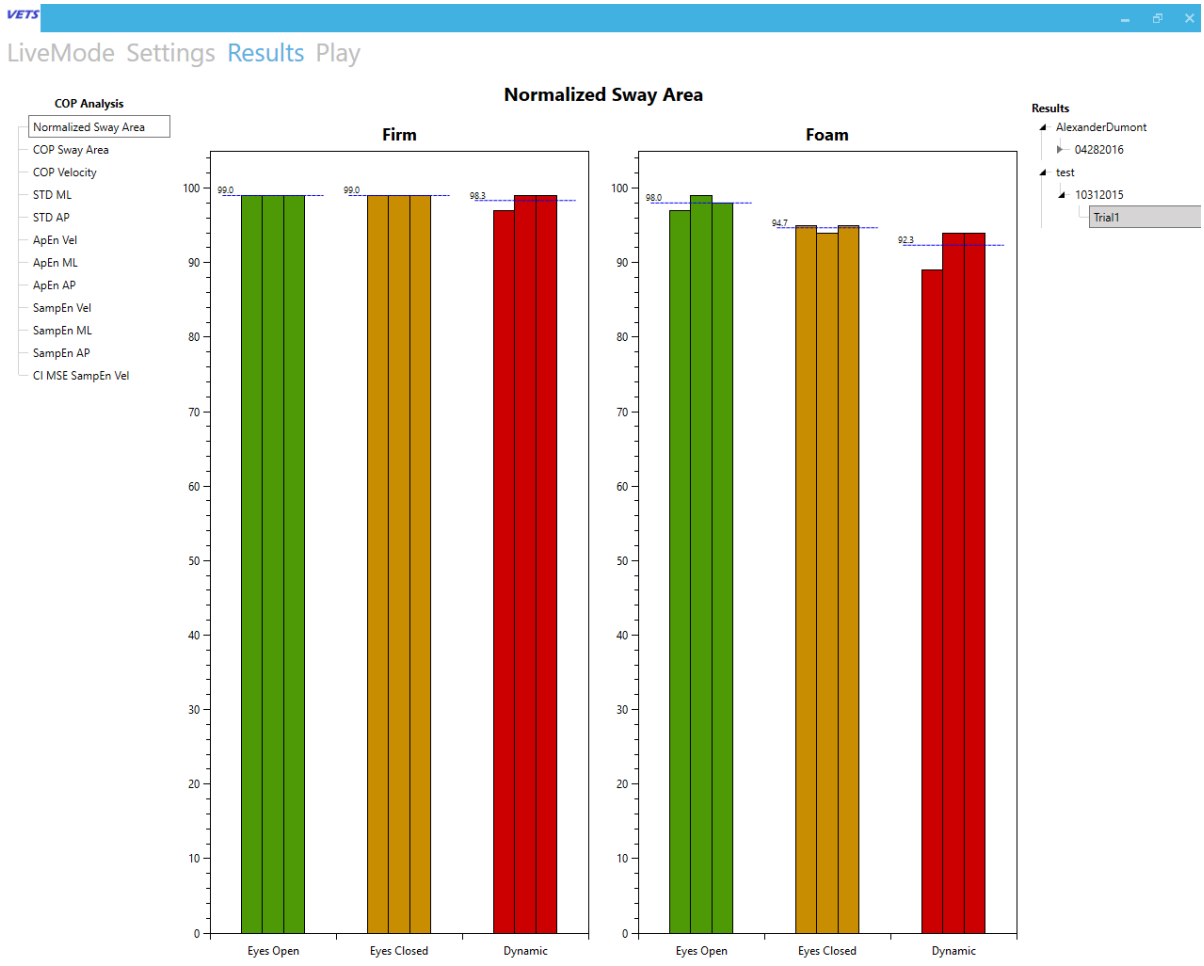
1. Eyes Open No Foam
2. Eyes Closed No Foam
3. Dynamic No Foam
4. Eyes Open Foam
5. Eyes Closed Foam
6. Dynamic Foam

The user can specify what trials he or she wants individually, or can use the two presets at the bottom right of the screen. If the user is not happy with the choice, he or she can individually delete

one trial by right-clicking on that trial and selecting delete or by deleting the entire list. The user is responsible for ultimately keeping track of the trials. For example, if he or she has chosen a foam condition, he or she should be careful to place a piece of foam on the WBB. In this aspect, there are no differences in the internal of the program except for labelling and differentiating between foam and no foam conditions.

Clicking the "Standard Trial Order" will produce 18 correctly labelled trials in a row, starting with $Firm \rightarrow EO, EC, Dyn$ and then $Foam \rightarrow EO, EC, Dyn$. Clicking on the "Random Trial Order" will randomize the trials completely, within no subsets, so the user may end up with foam→firm→foam conditions, which is not the easiest to deal with.

4 Results

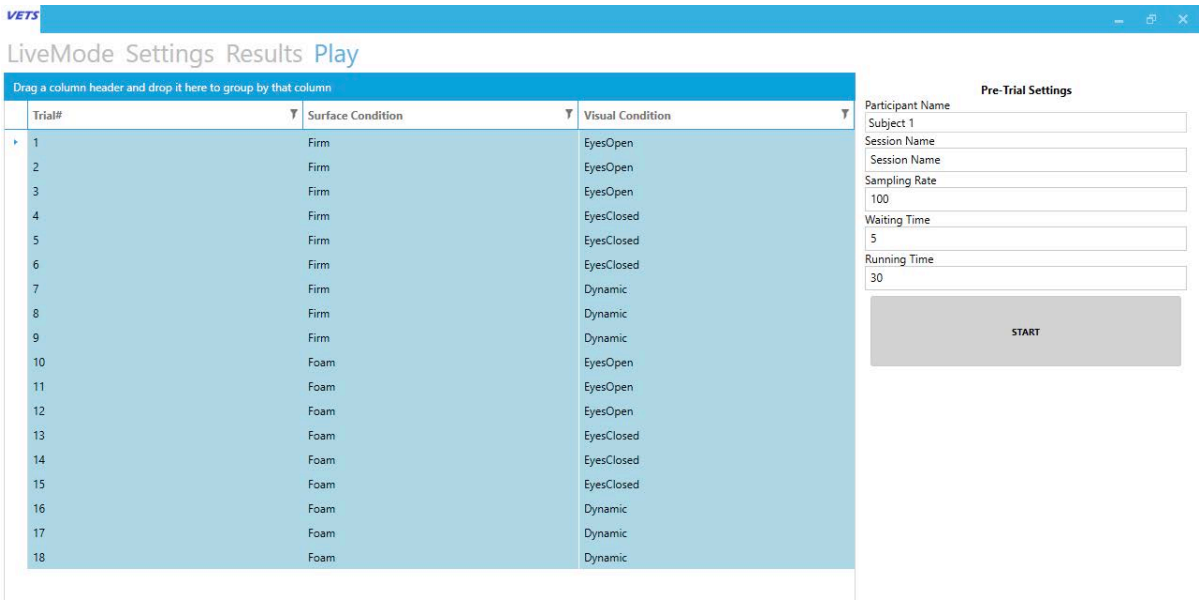


The results are presented above. To the right is a user selection mode. Clicking on a particular node will reveal the results for that node and all inferior nodes that descend from that node. If the user selects test, the result will display all trials under all dates in test. If the user choses Trial1, it will only display Trial1. There are several included metrics associated with the VETS program. These are:

1. Normalized Sway Area – Sway Area as calculated by Principal Component Analysis normalized to a maximum sway area that can occur without a fall (i.e. COP moves outside the base-of-support). The closer the raw sway area is value is to zero, the closer to 100% this value will be.
2. Center of Pressure Sway Area – This is the raw sway area as calculated by PCA. The user may consider alternative approaches to calculating sway area by Convex Hull, for example, by extracting the raw data.
3. Center of Pressure Velocity – This is a combination of mediolateral (ML) and anteroposterior (AP) directions to give Path Length, and then a summation of each individual Path Length.
4. Standard Deviation Medio-Lateral Direction – This is the standard sample deviation in the side to side direction of the balance board.
5. Standard Deviation Anterior-Posterior Direction - This is the standard sample deviation in the front to back direction of the balance board.
6. Approximate Entropy on Velocity – This is approximate entropy done to the Velocity before it is summed.
7. Approximate Entropy on Medio-Lateral Data - This is approximate entropy done to the raw ML data.
8. Approximate Entropy on Anterior-Posterior Data - This is approximate entropy done to the raw AP data.
9. Sample Entropy on Velocity – This is sample entropy done to the Velocity before it is summed.
10. Sample Entropy on Medio-Lateral Data - This is sample entropy done to the raw ML data.
11. Sample Entropy on Anterior-Posterior Data - This is sample entropy done to the raw AP data.
12. Complexity Index done on Sample Entropy on Velocity – this is a coarse-grained summation of sample entropy at $\tau = 1 - 20$.

The user may run a simulation. Once the simulation is finished, the Results menu will automatically show up with that subject's particular data.

5 Play



The Play Menu allows the user to check a readonly list of all the trials he or she wants to perform. The user can then specify the Participant Name, the Session Name, the Sampling Rate, the Waiting Time between the trials (set to 5s by default) and the Running Time for the trial (set to 30s by default). If any of theses text boxes are left empty, the user will not be able to click on START. The data entered in te text boxes will be the basis for storing the information and data on the tree source used in the results menu.

After the simulation is run, the user is obliged to go back to the settings page to re-chose the trials he or she wants for future tests.

6 Extracting the Results

The user may want to do his or her own analysis on the data. To do so, the user can orient himself or herself to the following address:

$$This\ PC \rightarrow Documents \rightarrow Vets \rightarrow Results$$

The names of all the participants will be stored in folder form. Clicking on a particular subject will reveal all the times that subject has participated in VETS studies. Clicking on any date will reveal the session name. Clicking once more will reveal 3 different folders labeled 10, 30, 100. The 10 and 30 folders are the data that has been pre-Butterworth filtered at 10 and 30 Hz respectively. The 100 folder is the raw data from the session. Clicking on any of these folders then reveals the Surface conditions and clicking on that reveals the Visual conditions. Finally, the data will be presented as and XML document one can easily access through MATLAB or any other analysis software.

7 FAQ

8 Further Sources of Information

There is an excellent website www.physionet.org for describing approximate entropy and sample entropy.

1. https://www.physionet.org/physiotools/ApEn/
2. https://physionet.org/physiotools/sampen/

There is also some code for MATLAB at:

3. http://www.mathworks.com/matlabcentral/fileexchange/35784-sample-entropy
4. http://www.mathworks.com/matlabcentral/fileexchange/26546-approximate-entropy

Which function quite well and can give an idea of how sample entropy and approximate entropy works. There is also a tutorial for multiscale entropy at:

5. https://physionet.org/physiotools/mse/

We used the complexity measure to get a single number back, which is described in various paper, though these one are a good start:

6. Busa, M. A., & van Emmerik, R. E. (2016). Multiscale entropy: a tool for understanding the complexity of postural control. *Journal of Sport and Health Science*.
7. Costa, M., Goldberger, A. L., & Peng, C. K. (2005). Multiscale entropy analysis of biological signals. *Physical review E*, *71*(2), 021906.

Appendix 2

VETS TECHNICAL MANUAL

Overview of VETS

VETS, first and foremost, is a visual scene renderer followed secondly by a data capture and recording engine. VETS operates through a multi-component system that communicates with each other as well as handle individual jobs. The following manual will break down each of these components and list out the jobs and functions they perform, as well as list any externally developed libraries (i.e. dependencies) that the components themselves may require.

For a brief overview of the operation of VETS, observe the following steps.

1. Upon loading and starting the program, VETs will use the WiimoteLib to facilitate a blue-tooth connection between the VETs and the Wii Balance Board.
    a. WiimoteLib is an open-source library design to allow a PC to communicate and use Wii blue-tooth based hardware. For more information, see the following website. (https://wiimotelib.codeplex.com/). This library allows real-time streaming of the center of pressure (CoP) data as a time series with a set sampling rate.
2. Users will be greeted with the Live Mode component; this is used to test if the Wii Balance Board is properly connected to the VETS systems and working, and provides a real time display of the data being received.
3. Users then select to the Settings component. This component allows users to set up a list of the conditions to be run. Conditions are separated into two major parts, visual and physical. Once components are selected they are stored in a Trials array list.
    a. The visual parts determine if the scene is rendered as a still image ('Eyes open'), not rendered at all ('Eyes closed'), or if the scene is rendered and rotating ('Dynamic')
    b. The physical parts determine if the protocol involves the use of a foam padding for the participant to stand on. Though not involved in data-gathering, this is used to help sort and organize the data for later readability.
4. Users then select the Play component. This component allows users to set up the specifics of the test as a whole. These options include the Participant's Name, the Session Name, the Sampling Rate (locked at 100 in future versions), the time given to wait between conditions, and the running time of each condition. When a user is ready they can select "Run Animation" and this proceeds to the Simulation component.
5. The Simulation component reads in the earlier created Trials array list, and splits the program off into three asynchronous systems.
    a. The major Simulation component handles the renderer and control of the conditions. It will run through the Trials array, rendering the scene and passing the individual details to all other involved components. This is the main render engine and is one of the heavier components in the system.
    b. RecordingService runs in the background and records the WiiBB data at a rate of 100hz. This data is stored into two separate object arrays. PointF is a native WiimoteLib structure that stores the X and Y data of a point. TimedPoint is a structure that mirrors PointF but adds in Time data as well, allowing for a timeline of the recording. This data is later passed to the WritingService.

c. WritingService runs in the background and receives data from both the RecordingService and the major Simulation component. It receives from the Simulation component the protocol-type and creates a directory based on the participant name, session name, and from the RecordingService the TimedPoint data. Once it has this data it begins to write out to two different log files. A .xml log file importable into Excel, and a raw data file that just contains the values.
d. On completion of a write, AnalysisService is run on the XML, this provides descriptive statistics of the collected data, which is used in the Results Component.

6. Upon completion, user is returned to the Results component. Here they can select from a list all participants and session names. The component uses the data from the XML to build charts containing mathematical and statistical analysis of the data, as well as offers an Export function to export this data into a clean and easy to read format.

This is the general procedure that a tester will take in use of the program, and the overall communication and state of the VETS system.

Changes from VETS LEGACY

All changes represent actively logged changes since 7/2016. The VETS system comprises of three different versions. The first version is referred to as VETS Legacy, and contains old code and recording algorithms for use with older machines and older sets of data. VETS is an upgraded version of VETS Legacy that uses a new data collection and recording algorithm to provide better data results analysis and time series data. VETS/OR is a new prototyped version of VETS recreating the VETS data collection and rendering engine in a 3D environment built in the Microsoft Unity 3D engine and making use of the Oculus Rift virtual reality headset for complete immersion.

The changes made to VETS are as follows.

- All instances of CogX/CogY were changed to standardized AP and ML dimensions as to prevent confusion with data.
- RecordingService has been upgraded to directly output to not only a XML file but a RAW data file, delimited by white space, for any additional data processing a user may wish to perform.
- A Refresh button has been added to the Results window that will rescan the Results directories for any new patients or information added.
- New art assets were created for the VETS engine, including standardized selection images for protocols as well as a brand new “Temple” scene that was created and rendered in the Unity engine.
- Numerous crashes, data loss scenarios, and incorrect recording situations were found and corrected.
- Optimization done on numerous components, as well as a limitation on the FPS (Frames Per Second) rendered in Simulation Mode. The Simulation Mode rendering is limited to 30 FPS.
- Optimization done on file read and writing situations, as well as a spinlock implementation to prevent rare cases of data loss.
- The VETs system will now broadcast what it is doing on the localhost through use of UDP. The purpose of this is to allow other systems to synchronize themselves to VETs

    - System broadcasts to port 11000 on IP 127.0.0.1 (localhost)
    - UDP data is sent out in the following format. "Visual" + "Physical" trial data. Example, if a scene is given the visual value of "Eyes Closed" and the involves the physical use of the foam padding the UDP signal will be encoded as "EyesClosedFoam".
    - When testing is paused, or ended, the UDP signal is encoded as "Off"
- With the above UDP programming, VETS/OR is able to synchronize with VETs for potential pilot testing.
- An export function has been added to the main Results page, allowing a user to export a participant's data into an easy to use PNG format for use in any assets they may choose to create.

VETS Data Output Format and VETS User Directory

VETS outputs and stores resources in a directory structure that is as follows.

C:\Users\<User Name>\Documents\VETS\

Images – Contains the main render for the Simulation View

Images – Contains all GUI based image assets used in the interface.

Resource – Use for building and storing user settings.

Results – A collection of all participant results gathered by VETs

VETS also separates the results directories as follows.

\Results\<Participant Name>\<Date of Recording>\<Session Name>\

<Data Rate>\<Physical Type>\<Visual Type>

Inside each of these directories are written any and all data gathered in that particular condition. Data is further sorted by exact time, down to the seconds as to prevent accidental overwriting. There are two data formats. A XML file that is directly importable in Excel, and a raw .txt file that able to be read in by any software or program for further analysis.

XML data contains the following.

<TrialData>

<RawData>

<DataPoint>

<ML> (float value of the WiiBB's X-axis Point)

<AP> (float value of the WiiBB's Y-axis Point)

<MilliSecondTimedStamp> Exact time data was recorded.

<DataResults>

<AnalysisResults>

<ResultPoint> (all of the following are a single float value)

<NormCopSway>

<CopVelocity>

<CopSwayPca>

<STDML>

<STDAP>

<ApenML>

<ApenAP>

<SampEnML>

<SampEnAP>

<CIMSESampEnVel>

<APENVel>

<SampEnVel>

Raw data is much simpler, as it was designed to simple store the data as-is with no additional formatting. Raw data is separated into three columns.

ML | AP | Milliseconds

All data that is recorded is then appended to the text file as it is received. The general purpose of the RAW file is provided unformatted data for use in filtering processes, MATLab, and any other programs that may be used to analysis the output.

Additionally, VETS/OR data is output using the same RAW data structure as above. VETS/OR supports two forms of data output, Euler and Quaternion. Unlike VETS, VETS/OR log files are stored in the following directory structure.

..\<User Inputted Directory>\<Participant Name>\<DateTime>\

VETS/OR allows the user to input the directory they wish to save in, by default this directory is C:\VetsVRLogs\ though it can be changed at runtime. VETS/OR data is stored in text files in the following format

<Participant Name> + <DateTime> + <Condition of Test> + <Euler/Quaternion>.txt

Euler formatted VETS/OR data consists of the following four columns.

Roll | Yaw | Pitch | Milliseconds

Quaternion formatted VETS/OR data consists of the following five columns

X | Y | Z | W | Milliseconds

VETS Code Structure

VETS Code Structure is separated into numerous modules and components. What follows is a description of the contents of each folder you will see upon loading the solution.

Bootstrapper

Contains bstrapper.cs; this file is used in the initialization of the VETS system and should not be touched unless you are adding additional hardware to the VETS recording system.

Components

Contains the individual xaml and code-behind for each of the main components. Here lies the LiveMode, Play, Results, Settings, Shared, and Simulation components. Also included is a Shared component that contains the information for the selection TABs, title bar, and formatting.

Controls

Basic UI controls are kept inside this folder, as well as the controls for the rendering engines. The code for rotating the scene render is containing within this folder, as well as the Results Viewer controls that you see in the Results Component.

Converters

Unused Legacy Code. Safe to ignore.

Events

VETS-based Events that are used in the trial collection and registration, checks if the simulation can be played (sanity checks), KeyPressedEvents, and other forms of interrupts and events used by the VETS system. This generally does not need to be touched.

Extensions

Unused. Safe to ignore.

Filters

Filters are provided here to perform on the collected data. There are two forms of filters. Filtering.cs filters the data by frequency, this is used to lower the sample rate if desired. The ButterworthFilter.cs is also used to lower the sample rate using the Butterworth algorithm.

Helpers

Helpers are used by the Results window to help databind the directory tree, explore and keep track of directories, and store the current write location for the VETS system during data recording.

Models

Models are the numerous data models used by the system. Some are unused and some are frequently used. A majority of these are used in the Analysis system to get the specific COP values found in the XML output. This also contains the TimedPoint structure used for recording the WiiBB as a

timeseries, the Trial object for storing condition information, and Vertex data for direct conversion from WiiBB to a 2D Point on a grid.

Modules

Contains only the initializer for the SimulationModule, and should not be touched.

Resource

Art assets used in building the InstallerShield setup for VETS.

Themes

Used by xaml, determines the coloration and overall design theme of the VETS

Util

Contains the services used by VETS, most of which are ran asynchronously. It contains the AnalysisServices, the BalanceBoard service, the data Export service, the ResultsWriter and WritingServices, and the RecordingService.

It also contains code used for the timing for scene length and pauses.

ViewModel

This is unused and has since been depreciated. Safe to ignore.

In the root directory of the VETS Solution you will find .dlls for libraries VETS uses. VETS makes use of the Telerik Windows Form system to provide an easy way to chart and graph the results from analysis. This directory also contains the OxyPlot for 2D Graph plotting.

Appendix 3

A portable virtual reality balance device to assess mild traumatic brain injury symptoms

A pilot validation study

W. Geoffrey Wright, PhD
Department of Physical Therapy
Department of Bioengineering
Temple University
Philadelphia, PA USA
wrightw@temple.edu

Jane McDevitt, PhD
Department of Kinesiology
Temple University
Philadelphia, PA USA

Kwadwo Osei Appiah-Kubi, PT
Department of Physical Therapy
Temple University
Philadelphia, PA USA

Abstract*— Mild traumatic brain injury (mTBI) following a head impact or blast exposure can cause diffuse injury to the brain, which can affect sensorimotor, cognitive, and emotional processes. Among the most common sensorimotor symptoms of mTBI is balance impairment. A commonly used assessments of balance following mTBI is the sensory organization test (SOT). This test has shown that postural deficits following head injury may be due to visual-vestibular processing issues, but it is less sensitive to unremitting symptoms that do not spontaneously resolve within a week. Our current project involves demonstrating validity and reliability of a novel low-cost, portable virtual reality-based balance screening device that employs established principles of sensorimotor reweighting and visual-vestibular integration. The goal is to determine if it can replace existing tools that are either prohibitively expensive or lack reliability or sensitivity. Methods: Healthy adults with no known musculoskeletal or neurological injury (n=27; 17 males, 10 females; 22.1±3.9 years) were tested to establish healthy norms. Individuals with mTBI (n=8; 4 males, 4 females; 20.0±1.7 years) were compared to the healthy norms. The new VR-based balance assessment system consists of a Wii balance board (WBB), a large screen television, and a custom-designed software user interface used to collect and process data. Subjects performed six upright postural tasks (three visual conditions either standing directly on the WBB or on foam placed on the WBB). Subjects viewed a virtual reality scene displayed on a 60" television. The three visual conditions were Static Scene, Dark Scene, and Dynamic Scene (Roll at 60 deg/s). The WBB recorded COP at 100Hz for 30 sec. Dependent variables included COP velocity, root mean square, and sway area. Subjects also performed the sensory organization test (SOT), which can be used as criterion-measures for intraclass correlations with the new device. Results: Preliminary data on healthy subjects validates effectiveness of the device to reduce postural stability as sensory input reliability and availability decreases. Additionally, our results reveal that individuals with mTBI have significantly worse balance scores on the new VR-device ($p<0.001$). This highlights its sensitivity to balance disturbance even if when testing a small sample. Comparison of the new device to SOT shows good criterion validity with ROC curves revealing sensitivity/specificity equal or higher than the SOT. COP sway area, velocity, and standard deviation of medial-lateral and anterior-posterior sway were all sensitive dependent variables. In conclusion, this study helps demonstrate that our new VR-based assessment tool is a valid measure for detecting balance related changes in neurologically impaired individuals and can potentially replace much more expensive equipment. Using postural control as an outcome measure of brain injury may help improve identification of individuals with sub-acute symptoms which may be used to guide rehabilitation and clinical decision-making.

Keywords— vestibular; visual; virtual environment; concussion

I. INTRODUCTION

Traumatic brain injury (TBI) affects over 2 million people per year in the U.S. with the largest percentage of these being mild TBI. Mild traumatic brain injury (mTBI), often referred to as concussion, can occur following a head impact or exposure to a bomb blast wave, and though the injury is usually not life-threatening, the effects may be serious. Some of the common symptoms of concussion are headache, cognitive deficits, blurry vision, dizziness, and posture deficits [1,2]. Postural assessment is one means to determine if a TBI victim is recovering, and common tests include subjective clinical assessment using the balance error scoring system (BESS) and more objective assessment using the Neurocom sensory organization test (SOT [3]). Although there is plenty of evidence that suggests these tests can be sensitive for detecting a concussion, there are drawbacks to each and changes that can be made that will improve clinical decision-making ability.

The SOT and BESS have both been found to be reliably sensitive to postural deficits during the first 3-5 days post-injury [3-9], however, a number of recent studies suggest there are postural and motor symptoms that last well beyond the typical 7-10 day spontaneous recovery period [10-12]. One of the reasons numerous concussive signs and symptoms go undetected is because patients learn to compensate when tested in a controlled setting using single-task clinical measurement techniques. This highlights one of the limitations of standard clinical assessments as well as computerized posturography; in

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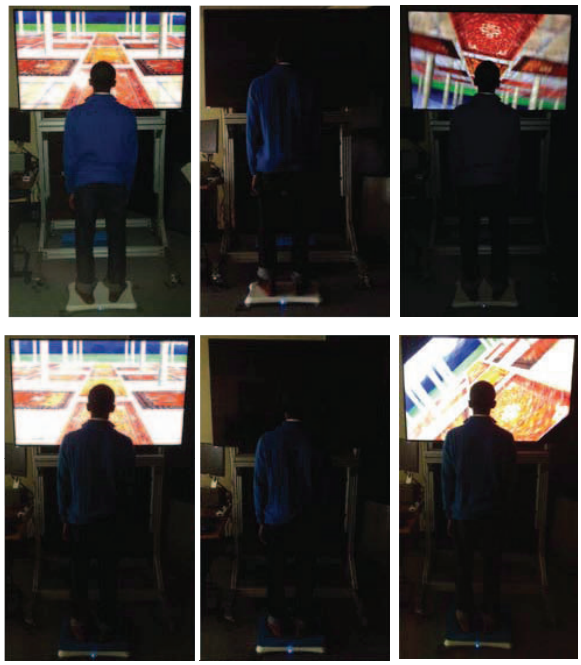

Fig. 1. VETS testing for the six conditions. Top row shows firm support conditions and the bottom row shows the foam support conditions. The three columns are EO while viewing a static VE scene, EC in front of a dark screen, and EO viewing a dynamic rotating scene.

order to identify persistent, but difficult to detect symptoms, the patient must be challenged and the assessment tool must isolate and test the deficient underlying neural processes. We propose to use dynamic virtual environments (VE) in a way that specifically challenges the visual-vestibular processes that help control posture. This approach builds on and refines the SOT, which is accepted by many as a *gold standard* for postural control testing.

Previous evidence using VR to detect balance changes following a head trauma show that dynamic visual motion poses particular difficulties for this population [12-13]. In a recent study by Haran and colleagues, when subjects who had been subjected to a series of subconcussive head impacts using a soccer heading paradigm, their balance was significantly worsened relative to controls. However, the deficit was only uncovered when the subject was in the most challenging condition in the VE, which was dynamic visual roll rotation while standing on an unstable sway-referenced surface [13]. In another balance study performed using VE, it was found that using roll motion, more so that pitch or yaw, was the most sensitive condition for detecting both acute and longer lasting balance deficits in concussed subjects [12]. Visual roll stimulation has been known to cause postural instability for decades [14] and optic flow in general is an important sensory cue for maintaining balance [15]. Moreover, symptom reports for concussed individuals often include sensitivity to visual motion and vestibular processing issues [16,17,5,18], therefore, testing visual-vestibular processing to detect whether concussion symptoms are present may prove to be more sensitive than assessments that do not test this.

The primary objective of this study was to validate a virtual reality based postural assessment device for detecting balance deficits in individuals with concussion that is affordable, portable, and accessible. To accomplish this we designed a novel VE tool that uses video-gaming technology to simulate a visual environment, which is viewed on a large commercially-available flatscreen television while high-resolution postural data is collected on a custom programmed Wii™ Balance Board (Nintendo) (*Fig. 1*). To change the stability of the support surface, we used standard foam pad often used in for balance testing in clinics. Traditional COP sway metrics (sway area, sway velocity, and sway variability) can be collected and analyzed by the new program and the statistical approach will incorporate methods of correlation, analysis of variance, and receiver operating characteristic curves to establish content and concurrent validity relative to the accepted criterion-related measures (i.e. SOT). If the device shows criterion validity relative to the SOT, then its real value as an alternative assessment tool lies in it affordability, accessibility, and ease of use, while still providing objective sensitivity and specificity for detecting concussion related postural deficits.

II. Methods

A. Subjects

Thirty-five active college student athletes were recruited to participate in this study (males=21; females=14). There were 27 healthy participants (22.1 ± 3.9 yrs; 1.73 ± 0.1 m; 72.4 ± 12.8 kg) and 8 concussed (20.0 ± 1.7 yrs; 1.74 ± 0.1 m; 72.5 ± 8.9 kg). All participants had been active in competitive sports for at least one year and the concussed athletes had experienced symptoms for 2 to 96 days, with 5 being acutely concussed (2-10 days). All participants self-reported having no recent orthopedic impairments that would negatively affect balance. The healthy athletes self-reported having no ear infection or vestibular, ocular or balance issues for the past month. Concussion in this study was defined as sustaining a pathomechanical event that induced one or more concussion signs or symptoms [1,2]. All subjects in the concussion group during the initial evaluation expressed that they had this event in addition to concussion signs and symptoms.

All subjects signed a Temple University IRB approved consent form in accordance with the guidelines of the Helsinki Accords. All subjects received monetary compensation for participation in the study. Participants completed the concussion questionnaire, which included background information such as history of concussion and general medical history including headache, vestibular and ocular issues. If recently concussed, then a description of injury, location of impact, and immediate and current signs and symptoms were also collected.

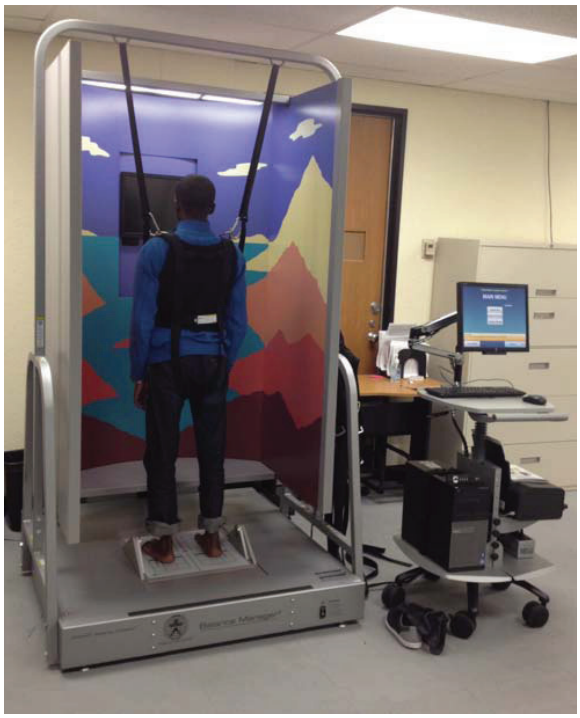

Fig. 2 Neurocom Smart Balance Master (Natus Medical, Inc.)

B. Instrumentation

1) Virtual Environment TBI Screen (VETS)

VETS is a novel postural assessment protocol that employs the use of virtual environment (VE) technology to simulate movement within a visual environment, which is viewed on a large commercially-available television (e.g. VIZIO E-Series Razor LED 60 inches) while high-resolution postural data is collected on a custom programmed user interface from a Wii™ Balance Board (Nintendo, Kyoto, Japan) communicated via wireless Bluetooth technology.

The Wii™ Balance Board (WBB) has been shown to be a valid tool for collecting reliable center-of-pressure (COP) data during human postural assessment [19-20]. Using our custom-programmed software interface, which collected COP data at 100 Hz sampling rate, the WBB was validated in-house relative to the SOT force plate ($r = 0.904\text{-}0.999$, $p<0.001$). Our visual stimulus uses a high-resolution digital snapshot taken of an immersive VE scene (VRCO, Virginia Beach, VA), which depicts a three dimensional scene of an outdoor temple with Greek columns, marble flooring, Persian rugs and a mountain range in the distance. The VE was passively rotated about the subject's roll axis to create a sense of self-motion in some conditions. The postural data collected by the VETS user interface includes COP velocity, root mean square (RMS) with means removed (i.e. standard deviation) in anteroposterior (AP) direction and the mediolateral (ML) direction, and COP sway area. COP sway area was found using a principal component analysis, which approximates an ellipse around the x-y COP data using the first two eigenvectors. COP velocity is calculated using the COP path length traveled in the x-y plane per time epoch (0.01 sec). An instantaneous COP velocity was calculated for each sample and the average instantaneous COP velocity per trial was reliably found to be equal to the quotient of the total path length divided by total trial time.

All VETS testing was performed in a dark room. The physical set-up has the front edge of the WBB placed at a distance of 40cm from the television screen. VETS protocol involves six conditions during which participants are instructed to look straight ahead and maintain an upright stance as stably as possible. The six conditions are (1) EO Firm – eyes open with stable support surface (i.e. WBB) and static visual scene, (2) EC Firm – eyes closed with stable support surface and dark screen, (3) DYN Firm – eyes open with a stable support surface and rotating scene, (4) EO Foam - eyes open with unstable support (Airex foam pad placed on top of the WBB) and stable visual scene, (5) EC Foam – eyes closed with unstable support and dark screen, and (6) DYN Foam – eyes open with unstable support and rotating scene (*Fig. 1*).

2) Sensory Organization Test (SOT)

All SOT testing was performed using the Neurocom Smart Balance Master System (*Fig. 2*, Natus Medical Inc., Pleasanton, CA). The SOT was designed to objectively identify abnormalities in the patient's ability to use the three sensory systems that contribute to postural control: somatosensory (proprioception), visual and vestibular. The SOT measures the vertical ground reaction forces produced from the body's center of gravity moving around a fixed base of support. The test systematically disrupts the sensory selection process by altering available somatosensory and/or visual information while measuring the ability to minimize postural sway in the anterior-posterior direction [21].

During the SOT protocol, participants were required to stand upright as stably as possible for 20 sec under 6 different testing conditions each repeated three times: (1) eyes open with stable support surface and visual surround, (2) eyes closed with stable support surface, (3) eyes open with sway-referenced visual input with stable support surface, (4) eyes open with unstable, sway-referenced support surface, (5) eyes closed with unstable, sway-referenced support surface, and (6) eyes open with both a sway-referenced support surface and a sway-referenced visual surround.

C. Procedure

All participants performed the VETS then the SOT protocols, respectively. Pilot testing revealed The VETS protocol involves testing the six conditions described above, in order, repeating each condition three times before proceeding to the next condition. Each condition lasts 30 sec with 5 sec between trials, except when switching from Firm to Foam conditions. Switching from Firm to Foam requires approximately 1 min for the subject to step off the WBB, add the foam pad, then adjust and re-measure the stance of the participant before condition 4 (EO Foam) can commence. The

TABLE I. MEANS AND STANDARD DEVIATIONS FOR HEALTHY AND CONCUSSED PARTICIPANTS

	Healthy		*Concussed*		
VETS COP	***Mean***	***SD***	***Mean***	***SD***	***p-value***
Sway Area					
EO - Firm	0.87	0.42	1.25	0.85	0.063
EC - Firm	1.40	0.74	3.46	5.10	0.292
DYN - Firm	3.44	1.71	17.4	18.8	0.001*
EO - Foam	3.33	1.36	5.48	5.67	0.073
EC - Foam	14.06	7.57	18.1	12.9	0.268
DYN - Foam	42.85	26.7	94.3	59.2	0.001*
Sway Velocity					
EO - Firm	1.93	0.35	1.91	0.28	0.849
EC - Firm	2.10	0.36	2.29	0.65	0.296
DYN - Firm	2.62	0.68	3.78	1.65	0.007*
EO - Foam	2.23	0.37	2.57	1.14	0.194
EC - Foam	4.20	1.36	4.39	1.33	0.750
DYN - Foam	7.02	2.80	9.54	3.48	0.044*
RMS ML					
EO - Firm	0.65	0.45	0.60	0.34	0.764
EC - Firm	0.71	0.41	0.64	0.40	0.671
DYN - Firm	0.90	0.46	1.42	0.86	0.032*
EO - Foam	0.95	0.64	0.89	0.54	0.810
EC - Foam	1.25	0.85	1.10	0.56	0.641
DYN - Foam	1.79	0.71	2.80	1.57	0.015*
RMS AP					
EO - Firm	2.96	1.25	2.83	2.23	0.846
EC - Firm	2.93	1.24	3.05	1.97	0.825
DYN - Firm	2.59	1.04	2.81	1.73	0.660
EO - Foam	1.99	1.24	2.63	1.56	0.240
EC - Foam	2.12	0.99	3.12	1.36	0.031*
DYN - Foam	2.25	0.96	2.83	1.30	0.176
SOT Equilibrium Scores					
Condition 1	95.7	1.21	94.8	1.18	0.038*
Condition 2	93.6	1.94	89.8	6.27	0.008*
Condition 3	92.4	2.99	86.0	5.84	0.001*
Condition 4	89.1	4.85	80.0	11.7	0.003*
Condition 5	70.8	7.31	67.2	9.90	0.305
Condition 6	69.1	8.66	64.7	12.9	0.269
Composite	82.4	4.36	77.1	7.90	0.021*

[a] *SD – standard deviation*
[b] *SOT (Sensory Organization Test)*
** significant at ≤ 0.05*

participant stood barefoot on the WBB with feet comfortably at shoulder width apart and the heel-to-heel distance was measured (~22cm). The participants were instructed to look at the center of the VE scene during eyes open and dynamic visual conditions. During dark conditions, subjects stood with their eyes closed while maintaining a similar head position as the other conditions. During all the testing, participants were instructed to stand with their arms resting by their sides while maintaining a stable, upright position. An experimenter stood behind them at all times to guard against falls.

The SOT testing required participants to stand barefoot on the Smart Balance Master System with feet placed in a standardized position, as suggested by the manufacturer's testing guidelines. The medial malleolus was lined up with the AP rotational axes of the support surface and visual surround. The lateral calcaneus was positioned in accordance with the guidelines prescribed by the participants' height. The standard testing conditions 1 – 6 were run with each one repeated three times. During all the testing participants were asked to rest their arms by their sides and maintain a stable, upright position being as still as possible for the duration of the 20 sec trial. The participant wore a safety harness, which was secured to the frame of the Neurocom device.

D. Data Analysis

The average of the three trials for each 6 conditions of the COP sway, COP velocity, RMS AP and RMS ML of the VETS for each participant and subsequently the overall averages were computed. Means and standard deviations were calculated for all dependent measures. Multiple repeated-measures analysis of variance (ANOVA) were performed to compare the significant differences of mean scores of all the conditions with its respective variables between the two groups to determine which tests were able to decipher between cases. Receiver operating characteristic (ROC) curves were used to determine the optimal sensitivity and specificity values for each dependent variable. First, the area under the curve (AUC) was calculated and a cutoff score was determined by choosing the value that maximized sensitivity and specificity. The AUC is an indicator of the overall value of a variable for accurate discrimination among all possible cut points for dichotomous categorizations of health status (i.e. concussed versus healthy). For SOT testing, we used the standard dependent variables provided by the Neurocom clinical output report. This postural sway dependent variable is based the total AP COP sway range. The variable is defined relative to a theoretical maximum sway range of 12.5 cm. The calculation is a percentage ranging from 0-100%. A score of 100% is the best performance, which means the participant's AP sway range was zero. A score of 0% equates to a large sway (12.5 cm) or a fall. All statistical analysis were conducted using SPSS software (version 22.0; IBM Corporation, Armonk, NY) and significance was set at 0.05. Bonferroni corrections to the alpha-level were applied as appropriate.

III. RESULTS

A. Health status between-group comparisons

Both the VETS and the SOT showed significant group differences between healthy and concussed subjects (Table 1). Using the VETS protocol all dependent variables were sensitive to health status (COP sway area, p=0.015; COP velocity, p=0.041; COP RMS AP, p=0.044; COP RMS ML, p=0.049). The SOT was also sensitive to health status, which is seen by comparing group SOT composite scores (p=0.021) or by repeated-measures ANOVA of all conditions (p=0.010). The SOT conditions 1-4 all exhibited significant between-group differences but the most difficult postural condition (Condition 6) was not sensitive to concussion status (p=0.27, n.s.).

B. Sensitivity and Specificity of VETS and SOT

In our study we used a known-groups analysis, whereby subjects with concussion were defined as having a mechanism of injury (i.e., a blow to the head or body) that resulted in one or more concussion signs and symptoms. Using this definition

we found significant AUC values in two VETS conditions and three SOT conditions. In the VETS protocol, the DV with the highest discrimination levels for detecting healthy subjects versus individuals with concussion was the COP sway area. Table 2 summarizes details of the ROC AUC scores for the SOT and VETS COP sway area. The ROC curve for COP sway area in the VETS condition DYN Firm reveals a significant AUC=0.83 (p=0.005) with a sensitivity of 75.5% and specificity of 92.6%. The ROC curve for COP sway area in the VETS condition DYN Foam was also significant (AUC = 0.77; p = 0.023) with a sensitivity and specificity of 62.5% and 92.6% respectively. Comparing these two conditions to the SOT, Condition 3 (Firm surface, sway-reference visual, which is comparable to VETS DYN Firm) had the highest discrimination with an AUC=0.85 (p=0.003) and a specificity of 87% and sensitivity of 84.6%. However, the most difficult balance condition in SOT, Condition 6 (Sway-reference surface, sway-reference visual, which is comparable to VETS DYN Foam), was not discriminatory for concussion status above chance (AUC=0.55, p=0.67). Also, the SOT composite score did not reach a significant discriminatory level for detecting concussed versus healthy (AUC = 0.71; p = 0.071) having a sensitivity of 62.5% and specificity of 69.2%.

C. Concurrent validity of VETS relative to SOT

We found that postural performance on the SOT gets progressively worse from Condition 1 to 6, which is in accordance with the established norms of this device. This was found for both healthy and concussed groups. Fixed surface conditions (Conditions 1-3) were significantly better than surface sway-referenced (Conditions 4-6) conditions ($p<0.01$), and as visual input was removed (EC – Cond 2 and 5) or sway-referenced (Conditions 4 and 6) performance decreased ($p<0.01$). On the VETS device, we found similar results, in that, conditions without foam were more stable than with foam ($p<0.001$). The EO conditions were more stable than EC, and DYN visual conditions were most unstable. All four COP dependent variables (sway area, sway velocity, RMS AP, and RMS ML) showed this pattern.

TABLE II. ROC SCORES FOR DISCRIMINATING CONCUSSED FROM HEALTHY PARTICIPANTS

Dependent Variable			
	***AUC*[a]**	***Cutoff value***	***p-value***
VETS COP Sway Area			
EO - Firm	0.72	0.99	0.059
EC - Firm	0.64	1.39	0.223
DYN - Firm	0.83	5.78	0.005*
EO - Foam	0.64	3.21	0.289
EC - Foam	0.61	14.3	0.366
DYN - Foam	0.77	72.3	0.023*
SOT[b] Equilibrium Scores			
Condition 1	0.74	95.5	0.044*
Condition 2	0.72	93.5	0.059
Condition 3	0.85	91.2	0.003*
Condition 4	0.76	85.5	0.026*
Condition 5	0.62	68.3	0.310
Condition 6	0.55	69.7	0.670
Composite	0.71	80.0	0.071

a. *AUC – Area under the curve*
b. *SOT (Sensory Organization Test)*
** significant at ≤ 0.05*

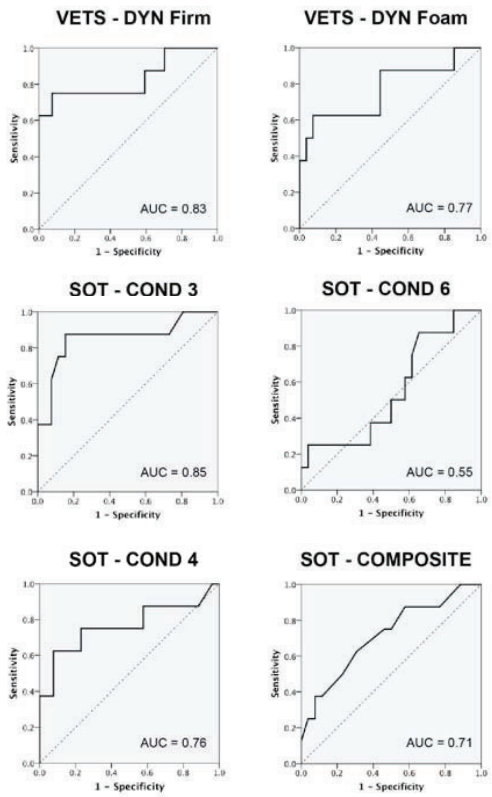

Fig 3. ROC curves for VETS COP sway area (top row) and SOT (lower rows). All have significant AUC, except SOT composite.

The Pearson product-moment correlations revealed strong to very strong negative relationships only for the VETS COP sway area relative to comparable SOT conditions, and only for the firm surface conditions. Surface sway reference conditions in SOT were not significantly correlated with foam surface conditions in VETS. Specifically, SOT condition 1 and VETS EO Firm were both postural tests conducted with a stable visual input while standing on a stable support surface. These conditions were significantly correlated ($r = -0.539$; $p=0.001$). SOT Condition 2 and VETS EC Firm were very strongly negatively correlated ($r = -0.846$; $p < 0.001$). SOT Condition 3 and VETS DYN Firm condition were modestly correlated for COP sway area ($r = -0.489$; $p = 0.003$). The unstable support surface conditions were not significant between SOT and VETS (Cond 4 vs. EO Foam, $r=-0.251$; Cond 5 vs. EC Foam, $r=-0.051$; Cond 6 vs. DYN Foam, $r=-0.084$).

IV. DISCUSSION

This pilot study validated a new VR-based device relative to the Neurocom SOT, which is considered the gold standard in instrumented postural assessment. Our custom-designed user interface successfully collects high-resolution COP data via wireless connectivity to a Wii balance board while visual and somatosensory input is altered across conditions. The new device showed good discrimination and significant differences

in performance between concussed and healthy individuals. Unlike the SOT and other VR postural assessment devices that have been reported in the literature, our device uses only affordable, commercially available electronic equipment and can be set up quickly and used with minimal training.

A. Establishing validity of the new VE balance device

Statistical tests were applied to establish concurrent and construct validity for the VETS balance device relative to the criterion measure, SOT. We used a known-groups methods to establish construct validity by calculating ROC curves to discriminate between individuals who reported a recent concussion with those who reported no concussions in the last 6 months. Overall, the VETS showed discrimination comparable to the SOT, outperforming it in some conditions.

The Pearson product-moment correlations were also applied to help determine concurrent validity. Before comparing the VETS protocol to the SOT, we tested the spatial and temporal resolution of the WBB when placed on top of the Neurocom forceplate. These tests showed that positional sway detection was highly correlated ($r = 0.904$-0.999) when both devices simultaneously collected COP data at 100 Hz sampling rate. Next we compared the conditions of the VETS protocol with those of the SOT. VETS and SOT were significantly correlated for the first three conditions in which a stable support surface was used. However, this was only true for the dependent variable COP sway area in VETS. These correlations were strong to very strong, which suggests that the VETS system is similar to the SOT in how it measures and assesses balance performance when the surface provides stable reliable somatosensory feedback. In the conditions which had unreliable surface support feedback (i.e. VETS Foam conditions and SOT surface sway-referenced conditions), a within subject significant correlation was not found. These results suggest although sway-referencing the support surface and standing on a foam surface both reduce the reliability of the surface somatosensory feedback, the effects on individuals' balance may be dissimilar. However, it should be noted that on average both the VETS COP sway variables (area and velocity) and the SOT measures showed that as the availability and reliability of the visual and somatosensory input was reduced balance got progressively worse. In other words, Condition 1 SOT performance was significantly better than Condition 2 was better than 3 and so on, while in the VETS protocol, EO Firm was better than EC and DYN and Firm support surface conditions were significantly better than Foam conditions. The fact that half the conditions showed significant correlations, and also two of the dependent variable of VETS matched the pattern of results found in the SOT, provide good evidence of concurrent validity of the VETS protocol.

B. Pathomechanisms underlying mTBI symptoms

The SOT is well-documented as being able to detect postural deficits following an mTBI [5] and here we provide further corroborating evidence of its usefulness. However, the results found using our VETS protocol suggest that an assessment tool for detecting mTBI symptoms may achieve greater sensitivity and specificity if it can specifically challenge the visual and vestibular processing deficits that seem to be concomitant sequelae of mTBI. It has been known for some time that vestibular processing deficits may be involved in the symptomatology of mTBI [22, 23]. Reliable clinical tests of vestibular function, such as the gaze stabilization test (GST), the dynamic visual acuity test (DVAT), and the dizziness handicap inventory (DHI) have all revealed reduced performance post-injury [22, 24, 25]. Further evidence for the involvement the vestibular system comes from how responsive it is to specialized treatment. Unremitting symptoms that do not resolve within one or two weeks following a head injury have been found to improve with vestibular rehabilitation [24, 26, 27]. In the visuomotor system, oculomotor tests of smooth-pursuit, convergence, saccadic control, and visuo-spatial attention are also known to be affected by an mTBI [28-30]. In fact, some of these visual and oculomotor deficits require as much as six months to fully return to normal [31].

Visual and vestibular processes are tightly linked via the vestibulo-ocular and optokinetic reflexes. Previous studies using the SOT showed a significant decrease in the SOT visual ratio for up to 2 days post-injury, before returning to normative levels [5]. In a complex multisensory task like postural control, the integration of visual and vestibular inputs are dependent on one another so even a minor diminution of the individual channels or the integration process can negatively affect postural stability. The current results from this study show that using a dynamic visual stimulus alter postural stability in healthy participants, but causes even greater problems for individuals with concussion. Additionally, we found that dynamic visual stimulation was sensitive to balance deficits in mTBI subjects who were more than 10 days post-injury in the three subjects.

C. Limitations and Future Plans

So far our study has only tested eight concussed individuals and our normative baseline for healthy controls is only a moderately large sample at n=27. Power analysis performed before beginning this project suggested that we would need a sample of 62 concussed and 50 healthy to establish the validity of this new device. Our results show our device is much more sensitive than anticipated. We have already found significant results and ROC curve analysis already shows "good" concussion detection ($AUC = 0.83$, $p<0.01$). Our next steps are to build a regression model using the most sensitive conditions and COP variables in the VETS protocol to optimize the level of discrimination.

Another limitation of this study is that we do not have a homogenous concussed population. Only half of the subjects fell within the acute period (<2 weeks), while the rest were greater than three weeks post-injury and were possibly suffering from post-concussive syndrome. As we build a larger test sample of brain injured subjects, we hope to be able to stratify our groups and be able to identify them according to their cutoff scores, or by identifying any differences in sensitivity to the various test conditions in the VETS protocol. A similar confound of heterogeneity may also be affecting the normative healthy baseline. Individuals in the healthy cohort were not excluded as long as they had not had a concussion in

the last 6 months. The long-term affects of concussion will be considered in our next steps, by collecting data on a healthy cohort who have never experienced a concussion.

Lastly, the SOT clinical report uses the built-in algorithms originally created by Neurocom. These values are based on one aspect of postural sway, which is the AP sway range. We focused on various AP and ML metrics derived from the COP data, so direct comparison of our metrics and those from the SOT could not be performed without getting access to the raw COP data. We also did not use the sensory ratios (i.e. visual, vestibular, somatosensory, and visual preference ratios), which may provide greater sensitivity to the deficits seen in individuals with mTBI. Once we have collected a larger sample of subjects and develop our own regression model, we will be able to compare the SOT sensory ratios to our own.

V. Conclusions

This study provides promising evidence of how emerging technology together with virtual reality can be easily integrated into the clinical setting and made accessible and user friendly. Future studies will build on this pilot study to try and improve its sensitivity and specificity, while also tying to use the device to gain greater insight into how the human sensorimotor system works.

Acknowledgment

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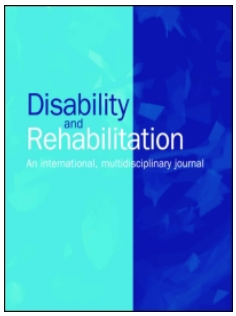
Appendix 4



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ORIGINAL ARTICLE

Assessing subacute mild traumatic brain injury with a portable virtual reality balance device

W. Geoffrey Wright[a,e], Jane McDevitt[b,c], Ryan Tierney[c], F. Jay Haran[d], Kwadwo Osei Appiah-Kubi[a] and Alex Dumont[e]

[a]Department of Physical Therapy, Temple University, Philadelphia, PA, USA; [b]Department of Athletic Training, East Stroudsburg University, East Stroudsburg, PA, USA; [c]Department of Kinesiology, Temple University, Philadelphia, PA, USA; [d]Department of Kinesiology, University of North Carolina-Greensboro, Greensboro, NC, USA; [e]Department of Bioengineering, Temple University, Philadelphia, PA, USA

ABSTRACT

Purpose: Balance impairment is a common sensorimotor symptom in mild traumatic brain injury (mTBI). We designed an affordable, portable virtual reality (VR)-based balance screening device (Virtual Environment TBI Screen [VETS]), which will be validated relative to the Neurocom Sensory Organization Test (SOT) to determine if it can replace commonly used postural assessments.

Methods: This preliminary study examines healthy adults ($n = 56$) and adults with mTBI ($n = 11$). Participants performed six upright postural tasks on the VETS and the SOT. Analysis of variance was used to determine between-group differences. Pearson's correlations were used to establish construct validity. Known-groups approach was used to establish classification accuracy.

Results: The mTBI cohort performed significantly worse than the healthy cohort on the new device ($p = 0.001$). The new device has 91.0% accuracy and an ROC curve with a significant area-under-the-curve (AUC = 0.865, $p < 0.001$). Conditions with dynamic visual stimulation were the most sensitive to health status. The SOT had an 84.8% accuracy and AUC =0.703 ($p = 0.034$).

Conclusions: The new VR-based device is a valid measure for detecting balance impairment following mTBI and can potentially replace more expensive and cumbersome equipment. Assessments that test visual-vestibular processing, such as VETS, increase sensitivity to mTBI-related balance deficits, which can be used to guide rehabilitation.

➤ IMPLICATIONS FOR REHABILITATION

- Emerging technology using virtual reality can be economically integrated into the clinical setting for easy testing of postural control in neurologically impaired populations.
- Tailoring postural assessments to include tasks that rely on visual and vestibular integration will increase the accuracy of detecting balance impairment following mild traumatic brain injury.

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Visual-vestibular processing; virtual reality; concussion; posture; sensory organization test

Introduction

Traumatic brain injury (TBI) affects over 2 million people per year in the United States with the largest percentage of these being mild TBI. Mild traumatic brain injury (mTBI), often referred to as concussion, can occur following a head impact or blast exposure, and though the injury is usually not life-threatening, the effects may be serious. Some of the common symptoms of concussion are headache, cognitive deficits, blurry vision, dizziness, and postural deficits.[1,2] Postural assessment is one means to determine if a concussion victim is recovering, and common tests include subjective clinical measures using the balance error scoring system (BESS) or a more objective measure, such as the Neurocom sensory organization test (SOT [3]). Although there is plenty of evidence that suggests both of these measures can be sensitive for concussion screening, there are drawbacks to each, thus, there is room to improve these postural assessment measures that could be used to improve clinical decision-making ability.

The SOT and BESS have both been found to be reliable and sensitive to postural deficits during the first 3–5 days post-injury,[3–9] however, a number of recent studies suggest there are postural and motor symptoms that last well beyond the typical 7–10 day recovery period.[10–12] One of the reasons numerous concussion signs and symptoms often go undetected is because patients can learn to compensate when tested in a controlled setting using single-task clinical measurement techniques. This highlights one of the limitations of standard clinical assessment measures as well as computerized posturography. In order to identify persistent, subacute symptoms, the assessment tool should be tailored to challenge the specifically deficient neural processes. We propose to use dynamic virtual reality (VR) scenes in a way that specifically challenges the visual-vestibular processes that help control posture. This approach builds on and refines the SOT, which is accepted by many as the "gold standard" for postural control testing, but shows only modest accuracy in concussion assessment and is very limited in sensitivity beyond the acute phase of injury.[13]

Previous evidence using VR to detect balance changes following a head trauma show that dynamic visual motion poses particular difficulties for this population.[12,14,15] It has been shown

CONTACT W. Geoffrey Wright, PhD wrightw@temple.edu Department of Physical Therapy, Temple University, Philadelphia, PA, USA
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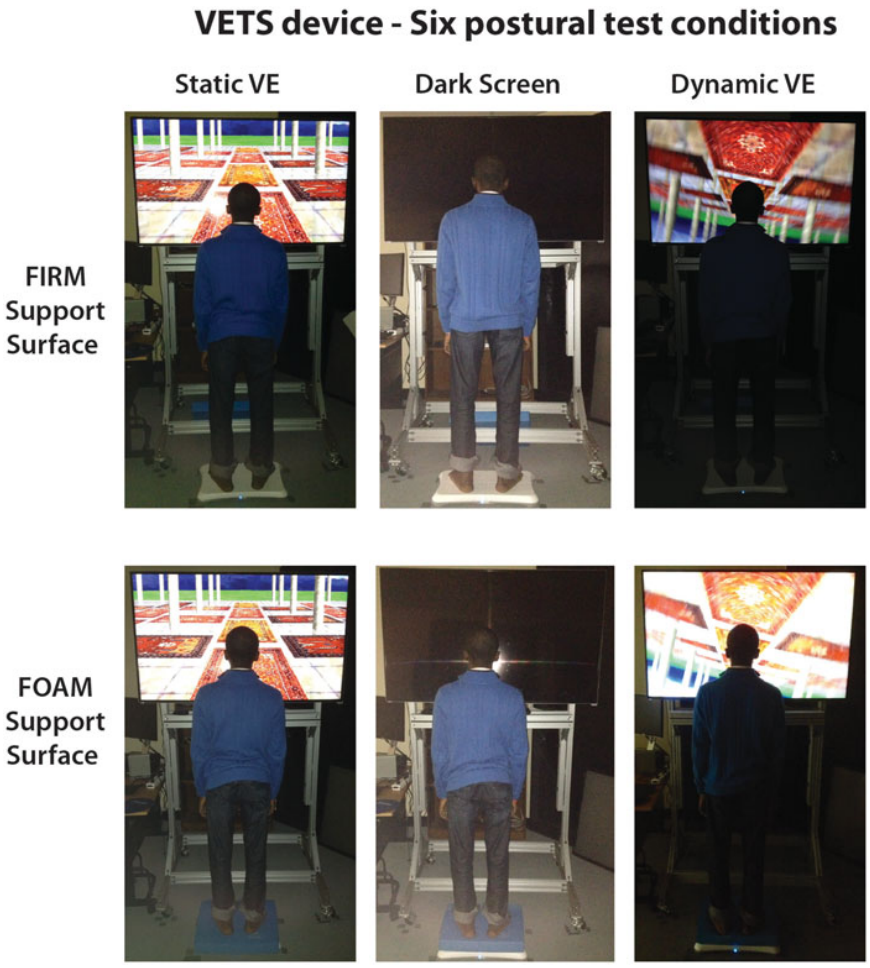

Figure 1. VETS – A VR-based balance device tests six conditions. Top row shows firm support conditions and the bottom row shows the foam support conditions. From left to right, the three columns are EO viewing a static VE scene, EC in front of a dark screen, and EO viewing a dynamic rotating scene.

that individuals subjected to a series of subconcussive head impacts using a soccer-heading paradigm showed significantly worsened balance relative to controls. However, the deficit was only uncovered when the experimental group was subjected to the most challenging VR condition, which included dynamic visual roll rotation while standing on an unstable sway-referenced surface.[14] In another balance study performed using VR, it was found that visual roll motion, more so than pitch or yaw, was the most sensitive condition for detecting both acute and longer lasting balance deficits in concussed subjects.[12] Visual roll stimulation has been known to cause postural instability for decades [16,17] and optic flow in general is an important sensory cue for maintaining balance [18]. Moreover, symptom reports for concussed individuals often include sensitivity to visual motion and vestibular processing issues,[5,19–21] therefore, testing visual-vestibular processing to detect whether concussion symptoms are present may prove to be more sensitive than assessments that do not.

In an attempt to apply this understanding of sensorimotor processing deficits concomitant with concussion, we developed a new portable virtual reality based postural assessment device for detecting the type of balance deficits specific to concussion. The custom-designed user-interface simulates and displays a virtual visual environment (Virtual Environment TBI Screen – VETS), which can be viewed on a large commercially available flat screen television while postural data is collected on a custom programmed Wii™ Balance Board (WBB – Nintendo, Kyoto, Japan) (Figure 1). To change the stability of the support surface, we used a standard foam pad, which are often used for balance testing in clinics. Traditional center-of-pressure (COP) metrics (sway area, sway velocity, and sway variability) can be calculated by the new program and were chosen because they are reliable [22] and examine important elements within the data time series that cannot be detected by sway range.

The main objectives of this effort build on our pilot work [23]: (1) to determine if there are statistical group differences between healthy and concussed participants, (2) to establish the construct and concurrent validity of the VETS relative to the criterion-measure SOT, and (3) to establish the discriminant accuracy of the VETS and SOT using "known-groups" methodology.

Methods

Subjects

Sixty-seven physically active (30 min of exercise at least three times a week) college students were recruited to participate in this study (males = 38; females = 29). Fifty-six healthy participants (22.6 ± 3.5 years of age; 1.73 ± 0.09 m; 71.1 ± 12.3 kg; females = 24) and 11 concussed (20.4 ± 1.8 years of age; 1.76 ± 0.11 m; 73.0 ± 6.4 kg; females = 5) were all active in competitive intramural (94%) or varsity (6%) sports for at least one year, and were proportionately represented in each group (intramural: healthy = 53,

concussed = 10; NCAA Division I athletes: healthy = 3, concussed = 1). Participants were excluded if they self-reported having had a musculoskeletal impairment within the last month that would negatively affect balance. Healthy participants were excluded if they self-reported having had an ear infection or vestibular, oculomotor or balance issues within the past month or had experienced a concussion within the last six months. Concussion in this study was defined as sustaining a pathomechanical event that induced one or more concussion signs or symptoms.[1,2] All subjects in the concussion group were interviewed by a certified athletic trainer or physical therapist during the initial evaluation and were included if they reported having an event within three months in addition to having experienced one or more concussion signs and symptoms (e.g., headache, dizziness, nausea, balance problems, difficulty concentrating, drowsiness, irritability. See Zurich Consensus Statement for complete list of symptoms [2]). All individuals in the concussion group had experienced symptoms for 2 to 90 days with six of them being subacute (>10 days post-injury).

All subjects signed a Temple University IRB approved consent form in accordance with the guidelines of the Helsinki Accords. All subjects received monetary compensation for participation in the study. Participants completed the concussion questionnaire, which included background information such as history of concussion and general medical history including headache, vestibular, and visual issues. If recently concussed, then a description of injury, location of impact, and immediate and current signs and symptoms were also collected.

Instrumentation

Virtual environment TBI screen (VETS)

VETS is a novel postural assessment measure that employs the use of VR technology to simulate movement within a visual environment, which is viewed on a large screen commercially available television (e.g., VIZIO E-Series Razor LED 60 inches) while center-of-pressure (COP) data is collected on a custom-programmed user interface from a WBB communicated via wireless Bluetooth technology.

The WBB has been shown to be a valid tool for collecting reliable COP data during human postural assessment.[24,25] The software interface and WBB, collected COP data at 100 Hz sampling rate and the data was validated in-house relative to the SOT force plate ($r = 0.90 - 0.99$, $p < 0.001$). Our visual stimulus uses a high-resolution digital snapshot taken of an immersive VR scene (VRCO, Virginia Beach, VA), which depicts a three dimensional scene of an outdoor temple with Greek columns, marble flooring, Persian rugs, and a mountain range in the distance. The VR scene was passively rotated about the subject's roll axis at 60°/s to create a sense of self-motion in the dynamic visual conditions. The postural data collected by the user interface includes COP velocity, standard deviation in anterior-posterior (AP) direction and the mediolateral (ML) direction, and COP sway area. COP sway area was found using a principal component analysis, which approximates an ellipse around the AP-ML COP data using the first two eigenvectors. COP velocity is calculated using the COP path length traveled in the AP-ML plane per time epoch (0.01 s). An instantaneous COP velocity was calculated for each sample and the average instantaneous COP velocity per trial was reliably found to be equal to the quotient of the total path length divided by total trial time.

All VETS testing was performed in a dark room. The physical set-up places the front edge of the WBB placed at a distance of 40 cm from the television screen in a completely dark room.

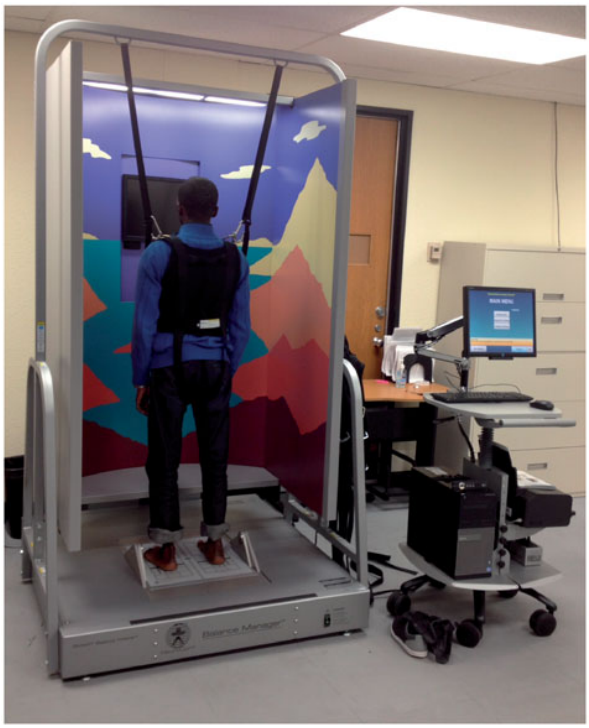

Figure 2. Neurocom Smart Balance Master (Natus Medical, Inc.).

The VETS testing involves six conditions during which participants are instructed to look straight ahead and maintain an upright stance as stably as possible. The six conditions are (1) EO Firm – eyes open with stable support surface (i.e., WBB) and static visual scene, (2) EC Firm – eyes closed with stable support surface and dark screen, (3) DYN Firm – eyes open with a stable support surface and rotating scene, (4) EO Foam – eyes open with unstable support (Airex foam pad placed on top of the WBB) and stable visual scene, (5) EC Foam – eyes closed with unstable foam support and dark screen, and (6) DYN Foam – eyes open with unstable foam support and rotating scene (Figure 1).

Sensory organization test (SOT)

All SOT testing was performed using the Neurocom Smart Balance Master System (Figure 2), Natus Medical Inc., Pleasanton, CA). The SOT was designed to objectively identify abnormalities in an individual's ability to use the three sensory systems that contribute to postural control: somatosensory (proprioception), visual, and vestibular. The SOT measures the vertical ground reaction and shear forces produced from the body's center of gravity moving around a fixed base of support. The test systematically disrupts the sensory selection process by altering availability/reliability somatosensory and/or visual information while measuring the ability to minimize postural sway in the AP direction.[26]

During the SOT, participants were required to stand upright as stably as possible for 20 s under six different testing conditions each repeated three times for a total of 18 trials: (1) eyes open with stable support surface and visual surround, (2) eyes closed with stable support surface, (3) eyes open with sway-referenced visual input with stable support surface, (4) eyes open with unstable, sway-referenced support surface, (5) eyes closed with unstable, sway-referenced support surface, and (6) eyes open with both a sway-referenced support surface and a sway-referenced visual surround.

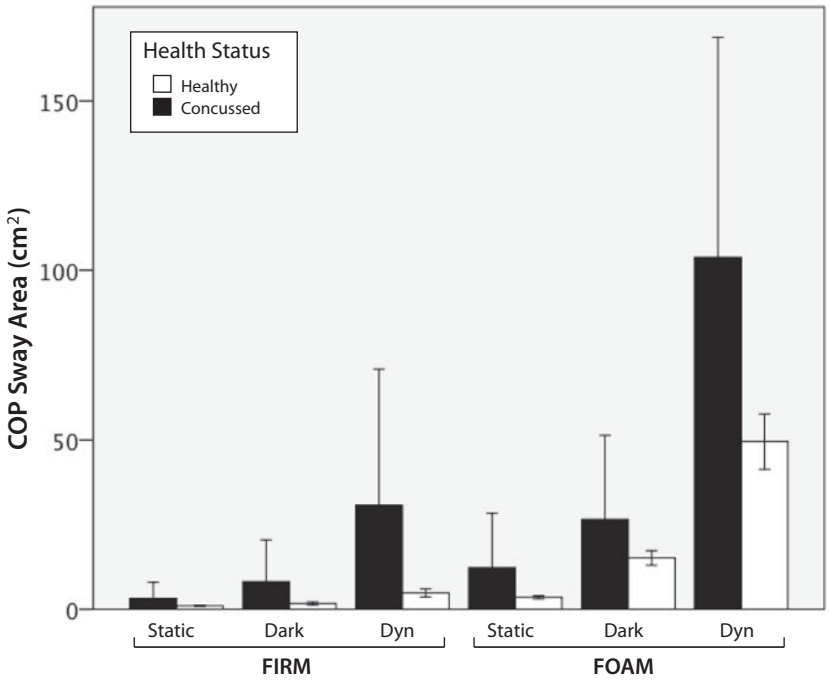

Figure 3. VETS COP sway area. Comparison of healthy (white) versus concussed (black) cohorts show significantly greater COP sway area in the concussion group. Error bars represent 95%CI.

Procedure

All participants performed the VETS then the SOT, respectively. Pilot testing revealed that there was no order effect ($n = 8$, $p > 0.25$, NS), therefore we subsequently tested VETS first for all subjects. The VETS involves testing the six conditions described earlier, in order, repeating each condition three times before proceeding to the next condition. This blocked sequential ordering was chosen since it has been validated as a part of the standard protocol used by the SOT. Each condition lasts 30 s with 5 s between trials, except when switching from Firm to Foam conditions. Switching from Firm to Foam requires approximately 1 min for the participant to step off the WBB, add the foam pad, then adjust and re-measure the stance of the participant before condition 4 (EO Foam) can commence. The participant stood barefoot on the WBB with feet comfortably at shoulder width apart and the heel-to-heel (middle calcaneus) distance was measured (22–25 cm). The participants were instructed to look at the center of the visual scene during eyes open and dynamic visual conditions. During dark conditions, participants stood with their eyes closed while maintaining a similar head position as the other conditions. During all the testing, participants were instructed to stand with their arms resting by their sides while maintaining a stable, upright position. An experimenter stood behind them at all times to guard against falls.

The SOT testing required participants to stand barefoot on the Smart Balance Master System with feet placed in a standardized position, as suggested by the manufacturer's testing guidelines. The medial malleolus was lined up with the AP rotational axes of the support surface and visual surround. The lateral calcaneus was positioned in accordance with the Neurocom guidelines prescribed by the participants' height. For heights <165 cm, a stance width 26 cm was used; for heights >165 cm, a stance width 30 cm was used (these measurements made between the left and right lateral calcaneus are comparable to the stance widths used in the VETS protocol, wherein stance width was measured between middle of the left and right calcaneus). The standard testing conditions 1–6 were run with each condition repeated three times. During all testing, participants were asked to rest their arms by their sides and maintain a stable, upright position being as still as possible for the duration of the 20 s trial. The participant wore a safety harness, which was secured to the frame of the Neurocom device.

Data analysis

Group differences in demographics were analyzed using independent sample two-tailed *t*-tests. Each of the six VETS conditions was tested three times for each participant from which an average was calculated. These within-subject, within-condition averages were used in mixed model repeated-measures analyses of variance (ANOVA), which were separately performed for each dependent variable (COP sway area, COP velocity, standard deviation of AP COP, and ML COP) to compare groups and within-subject visual and surface conditions ($2 \times 3 \times 2$). Violations of sphericity were checked by Mauchly's test, and in cases where a large violation of sphericity occurred a MANOVA was used [27]. A similar mixed model ANOVA was used on the SOT.

Pearson's correlations were used to establish the construct validity by comparing each comparable condition in the VETS and the SOT.

Known-groups methods, whereby group assignment was based on the aforementioned concussion criteria, was used to establish the classification accuracy of both the VETS and SOT. Two separate binary logistic regressions for dichotomous outcomes ("Enter Method" and "Forward Conditional") were run for each device (VETS and SOT) and "accuracy" was calculated as the sum of the true positives and true negatives divided by the total sample size. Logistic regression provided weighted coefficients (beta weights) for defining a regression model for each measure. Each regression model was then tested using receiver operating characteristic (ROC) curve analyses, from which area under the curve (AUC) was calculated. The AUC is an indicator of the overall value of a

variable for accurate discrimination among all possible cut points for dichotomous categorizations of health status (i.e., concussed versus healthy). For SOT testing, we used the standard dependent variables provided by the Neurocom clinical output report, which are based the total AP COP sway range. The variable is defined relative to a theoretical maximum sway range of 12.5 cm. The calculation is a percentage ranging from 0–100%. A score of 100% is the best performance corresponding to AP sway range equal to zero. A score of 0% equates to a large sway (12.5 cm) or a fall. Three trials are collected for each SOT condition and the Neurocom software automatically averages them to generate the equilibrium score for that condition. All statistical analyses were conducted using SPSS software (version 22.0; IBM Corporation, Armonk, NY) and significance was set at 0.05. Bonferroni's corrections to the alpha-level were applied as appropriate.

Results

Between-group comparisons

Demographics: The age, height, and weight of the healthy and concussed groups were not statistically different ($p > 0.10$, NS).

VETS: COP sway area was highly sensitive to health status group (Figure 3) showing a significant between-group effect ($F_{1,60} = 3.97$, $p = 0.002$, $\eta_p^2 = 0.28$). There was also a group-by-visual-by-surface condition interaction ($F_{2,64} = 3.36$, $p = 0.041$, $\eta_p^2 = 0.10$) due to the DYN visual conditions, which showed the largest between-group effect sizes (see Table 1).

COP velocity showed a significant between-group effect ($F_{6,60} = 2.35$, $p = 0.042$, $\eta_p^2 = 0.19$). A significant group-by-visual condition interaction was found in the firm support condition ($F_{2,64} = 4.62$, $p = 0.013$, $\eta_p^2 = 0.13$) due to the DYN Firm condition.

COP standard deviation in the ML direction showed only a nonsignificant trend in the interaction of group-by-visual condition ($F_{1,} = 2.75$, $p = 0.072$, $\eta_p^2 = 0.08$). The largest between-group effects sizes involved the DYN visual conditions.

COP standard deviation in the AP direction showed a significant between-group effect ($F_{1,64} = 7.02$, $p = 0.01$, $\eta_p^2 = 0.10$) and group-by-visual condition interaction ($F_{2,63} = 3.46$, $p = 0.038$, $\eta_p^2 = 0.10$), which was due to the DYN Firm condition.

SOT: The results of the SOT ANOVA did not show a significant between-group effect ($F_{1,64} = 2.01$, $p = 0.16$, $\eta_p^2 = 0.03$) or group-by-condition interactions ($F_{2,63} = 1.20$, $p = 0.31$, $\eta_p^2 = 0.04$). Because the surface conditions are inherently different tasks, we also explored each one separately, wherein only a group-by-visual condition interaction ($F_{1,64} = 9.47$, $p = 0.003$, $\eta_p^2 = 0.13$) was found to be significant, which was due to between-group differences in Condition 3 (Firm surface, Sway-referenced visual – see Table 1). The SOT composite score was not sensitive to health status ($t(64) = 1.34$, $p = 0.185$, *Cohen's* $d = 0.45$, Student's *t*-test for independent samples).

Concurrent and convergent validity of VETS relative to SOT

Sensory organization evidence in SOT and VETS: As has been well-established and again replicated in the current study, postural performance on the SOT gets progressively worse from Condition 1 to 6, in accordance with the established norms of this device. This was found for both healthy and concussed groups. Fixed surface conditions (Conditions 1–3) were significantly better than surface sway-referenced (Conditions 4–6) conditions ($F_{1,65} = 577$, $p < 0.001$). As visual input was removed (EC – Conditions 2 and 5) or became less reliable (sway-referenced visual in Conditions 4 and 6) postural performance decreased ($F_{2,64} = 69.7$, $p < 0.001$).

On the VETS device, we found a similar pattern, in that, conditions without foam were more stable than with foam ($F_{1,66} = 148$, $p < 0.001$). Also, as visual input was removed (EC) or made less reliable (DYN) postural stability decreased compared to the EO conditions ($F_{2,65} = 42.9$, $p < 0.001$). This pattern of behavior was evident in all four COP-dependent variables (sway area, sway velocity, AP-SD, and ML-SD) in the VETS device.

VETS-SOT correlations: The Pearson product-moment correlations revealed the expected negative relationships between the SOT conditions and the comparable VETS conditions (i.e., SOT Condition 1 compared to VETS Condition 1, SOT Condition 2 compared to VETS Condition 2, etc.). VETS COP sway area showed the strongest relationships with SOT conditions (Table 2). Only SOT Condition 1 (eyes open, stable support) and VETS Condition 1 (EO Firm) showed no significant correlations for any VETS COP metrics, which is likely due to the low between-subject variance in this easiest postural condition. The most challenging condition SOT and VETS condition (i.e., Condition 6) showed the highest *r* values for all four VETS COP metrics. COP sway velocity was not significantly correlated with any of its comparable SOT conditions, which is likely due to the construct differences in COP sway velocity (VETS) and AP COP sway range (SOT).

Table 1. Means and standard deviations for healthy and concussed participants.

	Healthy	Concussed	Between-group comparisons	
VETS	Mean ± SD	Mean ± SD	*p* Values	Effect size (η_p^2)
COP sway area (cm^2)				
EO – Firm	0.98 ± 0.91	3.19 ± 7.06	0.024*	0.076
EC – Firm	1.73 ± 1.55	8.13 ± 18.4	0.011*	0.097
DYN – Firm	4.86 ± 4.50	30.7 ± 59.9	0.002*	0.143
EO – Foam	3.53 ± 1.78	12.3 ± 1.77	0.007*	0.106
EC – Foam	15.2 ± 7.99	26.6 ± 7.99	0.037*	0.065
DYN – Foam	49.5 ± 30.5	104 ± 96.7	0.001*	0.158
COP sway velocity (cm/s)				
EO – Firm	2.54 ± 1.30	2.73 ± 1.22	0.676	0.003
EC – Firm	2.74 ± 1.40	2.82 ± 1.22	0.864	0.000
DYN – Firm	3.70 ± 2.12	5.18 ± 4.56	0.094	0.042
EO – Foam	2.83 ± 1.37	3.17 ± 1.47	0.469	0.008
EC – Foam	5.21 ± 2.76	5.09 ± 2.35	0.894	0.000
DYN – Foam	9.89 ± 6.20	10.7 ± 5.23	0.677	0.003
COP ± ML (cm)				
EO – Firm	0.25 ± 0.28	0.37 ± 0.52	0.284	0.018
EC – Firm	0.25 ± 0.26	0.37 ± 0.50	0.250	0.021
DYN – Firm	0.42 ± 0.28	0.83 ± 0.89	0.006*	0.112
EO – Foam	0.39 ± 0.25	0.68 ± 0.86	0.032*	0.070
EC – Foam	0.66 ± 0.30	0.86 ± 0.66	0.328	0.041
DYN – Foam	1.37 ± 0.66	1.90 ± 1.22	0.042*	0.063
COP ± AP (cm)				
EO – Firm	0.38 ± 0.31	0.46 ± 0.24	0.441	0.009
EC – Firm	0.50 ± 0.31	0.69 ± 0.48	0.093	0.043
DYN – Firm	0.63 ± 0.24	1.09 ± 0.97	0.002*	0.138
EO – Foam	0.55 ± 0.24	0.81 ± 0.56	0.014*	0.090
EC – Foam	1.13 ± 0.27	1.43 ± 0.77	0.020*	0.081
DYN – Foam	1.50 ± 0.27	1.88 ± 0.81	0.023*	0.078
SOT equilibrium scores				
Condition 1	95.4 ± 1.46	95.1 ± 1.27	0.515	0.007
Condition 2	92.8 ± 2.56	90.8 ± 5.68	0.067	0.051
Condition 3	92.0 ± 2.84	88.7 ± 5.16	0.004*	0.123
Condition 4	85.9 ± 8.55	82.0 ± 7.46	0.170	0.029
Condition 5	68.2 ± 8.57	67.7 ± 8.70	0.862	0.000
Condition 6	67.1 ± 10.4	65.2 ± 14.1	0.599	0.004
Composite	80.1 ± 5.34	77.5 ± 7.17	0.185	–

All *p* values are Bonferroni's adjusted for multiple comparisons.
SD: standard deviation; SOT: sensory organization test; VETS: virtual environment TBI screen.

Table 2. Correlations between VETS COP metrics and SOT.

	SOT					
VETS	Condition 1	Condition 2	Condition 3	Condition 4	Condition 5	Condition 6
COP sway area	−0.146	−0.358**	−0.398**	−0.251*	−0.331**	−0.497**
COP sway velocity	−0.003	−0.023	−0.140	−0.085	−0.120	−0.211
COP SD ML	−0.015	−0.066	−0.257*	−0.057	−0.181	−0.383**
COP SD AP	−0.129	−0.211	−0.377**	−0.051	−0.308*	−0.441**

SD: standard deviation; SOT: Sensory organization test; VETS: Virtual environment TBI screen.
*$p < 0.05$,
**$p < 0.01$.

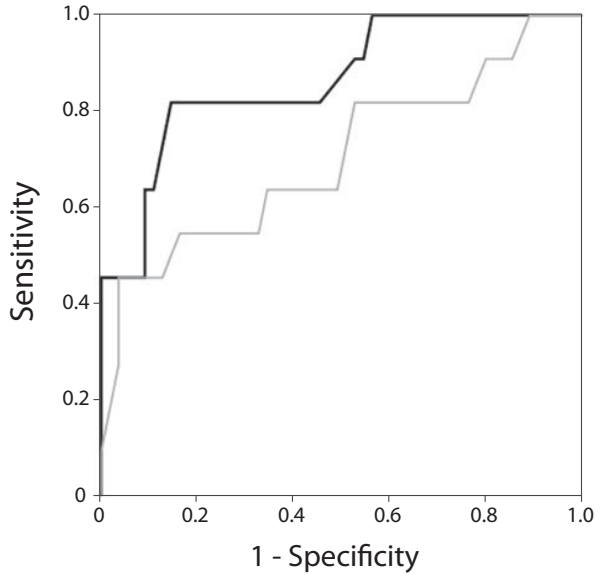

Figure 4. ROC curves generated using a logistic regression model. VETS COP sway area (thick black) shows greater discrimination than the SOT (thin gray), but both had a significant AUC with sensitivity and specificity better than chance (dotted diagonal line).

Discriminant accuracy of VETS and SOT

For VETS, since the ANOVA's for COP sway area were found to be most sensitive, we report the logistic regression results for this variable only. Using the "Enter" method, the logistic regression that included all six VETS posture conditions had the greatest accuracy (91.0%). Using the beta weights from the logistic regression, this linear model was used to generate a single value for each participant from which an ROC curve was calculated which was found to have an AUC = 0.865 ($p < 0.001$) (Figure 4). This model has very good ability to discriminate with a sensitivity of 81.8% and specificity of 85.7%. A second logistic regression for COP sway area using the forward stepwise conditional method found a significant beta weight ($p = 0.015$) for the DYN Firm condition, which resulted in a model with overall accuracy of 88.0%.

For SOT, a logistic regression using all six conditions was found to have 84.8% accuracy. The ROC curve derived from this linear model had an AUC = 0.703 ($p = 0.034$) (Figure 4), which has a sensitivity of 54.5% and a specificity of 83.6%. Condition 3 by itself was found to be the only significant predictor ($p = 0.011$) using the forward stepwise conditional method, but this resulted in a regression model with no greater accuracy than a null model with no predictors (i.e., 83.3%).

Discussion

This study reports the first step in the validation process of a new VR-based instrumented postural assessment (VETS). Our custom-designed user interface successfully collects high-resolution COP data via wireless connectivity to a Wii balance board while visual and somatosensory input is altered across conditions. The new device showed very good discrimination in detecting concussed versus healthy individuals. Unlike the SOT and other VR postural assessment devices that have been reported in the literature, our device uses only affordable, commercially available electronic equipment and can be set up quickly and used with minimal training. The WBB has been shown to be reliable and robust for measuring posturography,[24,25] and can be purchased new or used for less than $100. The use of a commercially available large flat screen television is the most expensive piece of equipment in our device, however, the price of electronics invariably drops overtime; the television used here is already 35% cheaper than when it was purchased 2 years ago. The custom-designed software allows for wireless acquisition of a high-resolution and high sampling rate (>100 Hz) data time series. Although the spatial resolution and the inability to collect shear force with the WBB does not qualify this equipment as research grade, it has been shown here that using the appropriate COP sway metrics together with well-chosen visual stimuli allows for very high assessment accuracy. A total cost of our device at under $1000 USD is one or two orders of magnitude cheaper than other specialized posturography equipment available on the market.

Establishing validity of the new VR balance device

We used a known-groups method to establish the classification accuracy (i.e., group discrimination) of the VETS by generating a logistic regression model that was then used to calculate ROC curves to discriminate between individuals who reported a recent concussion with those who reported no concussions in the last 6 months. Overall, for the sample tested the VETS showed better discrimination than the SOT. Analysis of both devices revealed the most accurate models required that all six conditions be included. Moreover, the models showed that the two conditions with unreliable visual input (i.e., VETS DYN Firm and SOT condition 3) had the best discriminability. How this relates to deficient visual and vestibular processing will be discussed below.

The Pearson product-moment correlations were also applied to help determine construct validity (i.e., convergent and discriminant validity). Before comparing the VETS to the SOT, we tested the spatial and temporal resolution of the WBB when placed on top of the Neurocom forceplate. These tests showed that positional sway detection was highly correlated ($r = 0.904$–0.999) when both devices simultaneously collected COP data at 100 Hz sampling rate. Next, we compared the conditions of the VETS with those of the SOT. The VETS and SOT were significantly correlated for all conditions except condition 1. This suggests the VETS device successfully accomplishes its design objective of quantifying postural sway metrics similarly to the SOT. Other evidence of the convergence of the VETS device with SOT is suggested by the fact that as the availability and reliability of the visual and

somatosensory input was reduced, balance progressively worsened. In other words, Condition 1 SOT performance was significantly better than Condition 2, which was better than Condition 3 and so on, while in the VETS, EO Firm was better than EC and DYN and Firm support surface conditions were significantly better than Foam conditions. These findings suggest that manipulation of the sensory integration process underlying postural control is occurring in the VETS, much as the SOT has been shown to do, which provides evidence of its construct validity.

Despite this convergent evidence, the correlations, albeit significant, can at the most only account for 25% of the variance between devices (i.e., $r_{max}<0.497$, see Table 2, SOT Condition 6 versus VETS DYN Foam). This divergence may, in part, be due to the fact that the VETS system manipulates the reliability of visual (i.e., dynamically rotated scene) and somatosensory (i.e., foam pad) input differently than the Neurocom SOT (i.e., sway-references the visual surround or support surface). This point will be discussed further in the next section. Another factor contributing to the discrimination of VETS from the Neurocom test is that the latter device uses the built-in algorithms to quantify the SOT equilibrium scores, which are based on only one aspect of postural sway, i.e., AP sway range. Whereas, the VETS device evaluates both AP and ML sway metrics. The choice of these COP metrics allowed us to more thoroughly quantify the time series signal. It was also necessary to run the VETS trials 10 s longer than the SOT trials to allow for the full effect of vection on postural stability to take effect.[16] These longer trials may have had the added benefit of getting at even lower frequency postural effects than with the SOT. Thus, although VETS shows comparable accuracy in its current application, it also separates itself from the Neurocom test in some important and beneficial ways.

Pathomechanisms underlying mTBI symptoms

The SOT has been shown to detect postural deficits following an mTBI,[5,13] however, the results found using our VETS suggest that an assessment tool for detecting mTBI symptoms may achieve greater sensitivity and specificity if it can specifically challenge the visual and vestibular processing deficits that seem to be concomitant sequelae of mTBI. It has been known for some time that vestibular processing deficits may be involved in the symptomatology of mTBI.[28–30] Reliable clinical tests of vestibular function, such as the gaze stabilization test (GST), the dynamic visual acuity test (DVAT) and the dizziness handicap inventory (DHI) have all revealed reduced performance post-injury.[21,28,30,31] Further evidence for the involvement of the vestibular system comes from how responsive it is to specialized treatment. Unremitting symptoms that do not resolve within one or two weeks following a head injury have been found to improve with vestibular rehabilitation.[30,32,33,34] In the visuomotor system, oculomotor tests of smooth-pursuit, convergence, saccadic control, and visuo-spatial attention are also known to be affected by an mTBI.[35–37] In fact, some of these visual and oculomotor deficits require as much as six months to completely return to normal.[38]

Visual and vestibular processes are tightly linked via the vestibulo-ocular and optokinetic reflexes. Previous studies using the SOT have shown a significant decrease in the SOT visual ratio for up to 2 days post-injury, before returning to pre-injury levels.[5,13] More recent evidence from a study that evaluated postural control using the SOT across several months of recovery in a large military cohort who had suffered an mTBI from blast exposure, found that their postural instability was primarily a result of impaired visual and vestibular integration.[39] In a complex multisensory task like postural control, the integration of visual and vestibular inputs are highly dependent on one another, so even a minor alteration of the input from individual sensory channels or a deficiency in the sensory integration process can negatively affect postural stability.[40] By comparing performance in specific conditions, we were able to rule out the effects of individual sensory channels on balance. Specifically, by comparing performance to the baseline condition (i.e., eyes-open firm condition), the concussed group could effectively use, (1) somatosensory input in the eyes-closed firm surface condition (2) visual input in the eyes-open foam surface condition (or EO sway-referenced surface in the SOT), and (3) vestibular input in the eyes-closed foam surface condition (or EC sway-referenced surface in the SOT). However, the dynamic visual conditions, especially on a stable support surface, were found to be most affected. This points to a deficit in visual-vestibular processing.[16] It is notable that this also held true for those who were subacute in our sample. In five participants who were more than 10 days post-injury, we found this condition still discriminated between groups.

This potential visual-vestibular processing deficit raises an important distinction between the conditions in the SOT and VETS with unreliable visual feedback, which was first mentioned in the previous section. Visual sway-referencing used in the SOT has the effect of minimizing optic flow by stabilizing the visual scene relative to the movement of the test participant (i.e., participant-fixed visual frame of reference), whereas the dynamically rotating visual scene used in VETS increases optic flow. Since it has been reported in a number of studies now that individuals with brain injury are sensitive to visual motion,[12,20,21,34] exposing these individuals to dynamic visual stimulation likely has a more disturbing effect on postural control than visual sway-referencing. It has more specifically been shown that roll-plane motion seems to be the most destabilizing for this injured cohort.[12] Although roll-plane motion has also been shown to be more posturally destabilizing than other directions of motion in healthy individuals,[17] the reason roll stimulation in general is most provocative remains unclear. We can only speculate that it perhaps derives from the regularity of exposure to pitch and yaw optic flow relative to roll during the normal process of moving about in one's environment. However, why this differentially affects brain injured individuals is also unclear. We suggest that it is related to the areas of the brain commonly injured in concussion, such as the midbrain and temporo-parietal regions,[41] areas that are integral to oculomotor control and visual motion processing, respectively. Visual-vestibular processing regions such as the parieto-occipital and parietal insular vestibular cortex are thought to be reciprocally innervated and connect to the vestibular nuclei, which have descending tracts that play an important role in maintaining upright dynamic postural stabilization.[40,42]

Limitations and future plans

So far our study has only tested eleven concussed individuals and this was a rather heterogenous concussed population. Only half of the participants fell within the acute period (<2 weeks), while the rest were greater than three weeks post-injury and were possibly suffering from post-concussive syndrome. As we build a larger test sample of brain injured subjects, we hope to be able to stratify our groups according to time-since-injury. Similarly, lack of homogeneity may also be affecting the normative healthy baseline. Individuals in the healthy cohort were excluded only if they had not had a concussion in the last 6 months and reported no more than three diagnosed concussions ever. Although the medical history interview specifically asked participants if they knew

what a concussion was, at least a few participants said they had been hit hard enough to be dizzy and get a headache on a number of occasions while playing their sport, but still reported never having had a diagnosed concussion. This represents a known problem in establishing a normative baseline in concussion research, in that getting accurate subjective report data from the "normal" population is not only difficult for the lay population to define, but it is also difficult for the experts to operationalize. Despite these limitations, our early results show the new VR-based device has good concurrent validity relative to the SOT, it detects the significant between-group differences, and it has very good discriminability (accuracy = 91%). Because our findings show that similar deficits of balance control and visual-vestibular processing may be present in both the acute and subacute phases of injury, this helps shed light on the timeline of underlying pathomechanisms, which helps to generalize the findings across stages of recovery.

In conclusion, this study provides promising evidence of how emerging technology can be easily integrated into the clinical setting and made accessible and user friendly. The new VR-based device is a valid measure for detecting balance impairment following mTBI and can potentially replace more expensive and cumbersome equipment. Additionally, we found evidence that using tests specifically focusing on visual-vestibular processing may increase sensitivity to mTBI-related symptoms. By increasing sensitivity and specificity of our assessment tools, we also increase the clinician's decision-making accuracy and ability to guide rehabilitation. Future steps will involve incorporating these new balance assessments with tests that incorporate cognitive and emotional assessments, in order to maximize sensitivity and specificity with a multifaceted approach to mTBI assessment.

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Disclosure statement

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Appendix 5

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Vestibular and Oculomotor Assessments May Increase Accuracy of Subacute Concussion Assessment

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Vestibular and Oculomotor Assessments May Increase Accuracy of Subacute Concussion Assessment

Authors

J. McDevitt[1], K. O. Appiah-Kubi[2], R. Tierney[3], W. G. Wright[2,4]

Affiliations

[1] Athletic Training, East Stroudsburg University, East Stroudsburg, United States
[2] Physical Therapy, Temple University, Philadelphia, United States
[3] Kinesiology, Temple University, Philadelphia, United States
[4] Bioengineering, Temple University, Philadelphia, PA, United States

Key words
- near point convergence
- optokinetic stimulation
- gaze stabilization test
- concussion
- mild TBI
- BESS
- SOT

Abstract

In this study, we collected and analyzed preliminary data for the internal consistency of a new condensed model to assess vestibular and oculomotor impairments following a concussion. We also examined this model's ability to discriminate concussed athletes from healthy controls. Each participant was tested in a concussion assessment protocol that consisted of the Neurocom's Sensory Organization Test (SOT), Balance Error Scoring System exam, and a series of 8 vestibular and oculomotor assessments. Of these 10 assessments, only the SOT, near point convergence, and the signs and symptoms (S/S) scores collected following optokinetic stimulation, the horizontal eye saccades test, and the gaze stabilization test were significantly correlated with health status, and were used in further analyses. Multivariate logistic regression for binary outcomes was employed and these beta weights were used to calculate the area under the receiver operating characteristic curve (area under the curve). The best model supported by our findings suggest that an exam consisting of the 4 SOT sensory ratios, near point convergence, and the optokinetic stimulation signs and symptoms score are sensitive in discriminating concussed athletes from healthy controls (accuracy = 98.6%, AUC = 0.983). However, an even more parsimonious model consisting of only the optokinetic stimulation and gaze stabilization test S/S scores and near point convergence was found to be a sensitive model for discriminating concussed athletes from healthy controls (accuracy = 94.4%, AUC = 0.951) without the need for expensive equipment. Although more investigation is needed, these findings will be helpful to health professionals potentially providing them with a sensitive and specific battery of simple vestibular and oculomotor assessments for concussion management.

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Correspondence
Dr. W. Geoffrey Wright
Physical Therapy
Temple University
3307N. Broad St
Philadelphia
United States 19130
Tel.: +1/215/204 5152
Fax: +1/215/707 7500
wrightw@temple.edu

Introduction

Concussion experts have suggested that clinicians use a multi-faceted approach to assess concussion [9, 14, 18, 30]. Authors of recent concussion position statements recommend including signs and symptoms (S/S), cognitive, and balance assessments into concussion management strategies [4, 18, 30]. Dizziness is a symptom endorsed by over 50% of concussed athletes [27] and is associated with a greater than 6-fold increased risk for prolonged recovery [27]. Common testimonial of dizziness suggests that concussion causes dysfunction with vestibular and/or visual pathways. This has led to researchers examining the diagnostic value of vestibular and oculomotor assessments in concussion management [1, 9, 32].

Vestibular and oculomotor testing for concussion screening is relatively new, but has shown promise. Mucha et al. (2014) assessed oculomotor function using near point convergence (NPC), smooth pursuits, and rapid volitional saccades, while, the vestibular ocular reflex (VOR) function was assessed using horizontal and vertical gaze stabilization (rapid head and eye movement) [32]. This study reported cutoff scores, which showed that an NPC distance over 5 cm increased the likelihood of correctly identifying concussed individuals by 38% and endorsing more than 2 symptoms on any of their vestibular/oculomotor assessments increased it by 50% [32]. The vestibular and oculomotor systems are important in sensing angular and linear acceleration of the head and eyes, which enables a moving individual to maintain gaze on a stable target or a stationary individual to focus on a moving target.

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Combining these assessments with others that examine whole-body behavioral output of vestibular, visual, and somatosensory integration (e.g., postural balance) may increase sensitivity and greatly improve concussion management.

Postural assessment is recommended in the National Athletic Trainer's Association concussion position statement [4,18,30]. Common tests include the Balance Error Scoring System (BESS [17]) or the Sensory Organization Test (SOT [33]). There is limited data on the reliability and validity of the SOT to determine postural instability following a concussion [33]; however, both the SOT and BESS have been reported to be sensitive to postural deficits during the first 3–5 days post-injury [5,16,17,28, 33,36,37]. The BESS has been shown to return to normal or baseline scores within 5 days post-injury [16,28]. However, a number of studies, suggest there are postural and motor symptoms that last well beyond the initial 7–10 day recovery period [2,23,43]. The ability of these postural assessments to identify deficits in later stages of recovery is limited, but it may be augmented by the inclusion of vestibular and oculomotor testing.

Currently, there is no agreed upon standard by which to assess individuals following a concussion [18,50]. There are many balance, vestibular, and oculomotor tests that an athletic trainer could use for the assessment of a concussion, but this can be time-consuming for both the clinician and the athlete. The purpose of this study was to investigate the usefulness of 10 assessments for detecting symptoms following a concussion, which were specifically selected because they depend on vestibular, oculomotor, or sensorimotor processing.

Materials and Methods

Study design

A cross-sectional research design with a known-groups approach (i.e., concussion vs. healthy) was implemented to determine the best balance, vestibular, and oculomotor assessment model to assess the presence of concussion symptoms.

Subjects

72 active college student athletes participating in either a Division I NCAA sport or college intramural team were recruited to participate in this study (42 males; 30 females) aged 21.5±3.4 years. There were 60 healthy participants (21.7±3.6 years; 68.3±3.7 in; 71.4±12.2 kg) and 12 concussed (20.5±1.8 years; 69.4±4.2 in; 72.8±8.4 kg). All participants had been active in competitive sports (17 different sports; **Table 1**) for at least one year and the concussed athletes had experienced symptoms for 4–90 days, with 6 participants being acutely concussed (2–10 days). All participants self-reported having no recent orthopedic impairments that would negatively affect balance. The healthy athletes self-reported having no ear infection or vestibular, oculomotor or balance issues for the past month. Concussion in this study was defined as sustaining a pathomechanical event that induced one or more concussion S/S [18,30]. All participants in the concussion group were evaluated by a certified athletic trainer (JM, RT) and during the initial evaluation verbally reported that they experienced a recent pathomechanical event followed by one or more concussion S/S.

All participants signed the Temple University Institutional review board approved consent form in accordance with the guidelines of the Helsinki Accords. All subjects received monetary compensation for participation in the study [19]. Participants completed the concussion questionnaire, which included background information such as history of concussion and general medical history including headache, vestibular and visual issues. If recently concussed, then a description of injury, location of impact, and immediate and current S/S were also collected.

Table 1 Sport participation data by group.

Sport n (%)	Concussed *n*=12	Control *n*=60
Australian Football	0 (0)	1 (1.7)
Baseball	0 (0)	1 (1.7)
Basketball	1 (8.3)	11 (18.3)
Fencing	1 (8.3)	0 (0)
Field Hockey	1 (8.3)	1 (1.7)
Figure Skating	0 (0)	1 (1.7)
Flag Football	3 (25)	3 (5)
Football	0 (0)	1 (1.7)
Gymnastics	1 (8.3)	2 (3.3)
Ice Hockey	1 (8.3)	3 (5)
Lacrosse	0 (0)	3 (5)
Mixed Martial Arts	0 (0)	1 (1.7)
Rugby	1 (8.3)	3 (5)
Soccer	1 (8.3)	21 (35)
Ultimate Frisbee	0 (0)	2 (3.3)
Volleyball	0 (0)	6 (10)
Not Reported	2 (17)	0 (0)

Instrumentation

Sensory organization test (SOT)

All SOT testing was performed using the Neurocom (Natus Medical Inc., Pleasanton, CA). The SOT was designed to objectively identify abnormalities in the participant's ability to use the 3 sensory systems that contribute to postural control: somatosensory (proprioception), visual and vestibular. The SOT measures the vertical ground reaction and shear forces produced from the body's center of gravity moving around a fixed base of support. The test systematically disrupts the sensory selection process by altering available somatosensory and/or visual information while measuring the ability to minimize postural sway in the anterior-posterior direction [34].

The SOT protocol requires participants to stand upright as stably as possible for 20 s under 6 different testing conditions each repeated 3 times: (1) eyes open with stable support surface and visual surround, (2) eyes closed with stable support surface, (3) eyes open with sway-referenced visual input with stable support surface, (4) eyes open with unstable, sway-referenced support surface, (5) eyes closed with unstable, sway-referenced support surface, and (6) eyes open with both a sway-referenced support surface and a sway-referenced visual surround.

The participants were tested barefoot with feet placed in a standardized position, as suggested by the manufacturer's testing guidelines (i.e., the medial malleolus was lined up with the anterior-posterior rotational axes of the support surface and visual surround, and the lateral calcaneus was positioned in accordance with the guidelines prescribed by the participants' height). The standard testing conditions were run in order (i.e., 1, 2, …, 6) with each condition repeated 3 times before proceeding to the next one. During all trials participants were asked to rest their arms by their sides and maintain a stable, upright position being as still as possible for the duration of the 20 s trial. The

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participant wore a safety harness, which was secured to the frame of the Neurocom device.

The Neurocom device calculates the SOT composite score as a weighted average of all 6 conditions to determine the overall level of performance as a percentage from 0–100, with better performance represented as a higher score and a fall scored as 0. The Neurocom software also calculates the sensory ratios, which estimate the participants' ability to utilize each type of sensory input to maintain balance. The somatosensory ratio is the quotient of condition 2 over condition 1. The visual ratio is the quotient of condition 4 over condition 1. The vestibular ratio is the quotient of condition 5 over condition 1. The visual preference ratio is the sum of conditions 3 and 6 divided by the sum of conditions 2 and 5. This ratio represents the degree to which a participant relies on visual input to maintain balance even if the visual input is unreliable.

Balance error scoring system (BESS)

The BESS test provides an objective measure of postural stability by testing balance in a series of 6 stances. The 6 conditions, always tested in the same order, are 3 stances (double-leg, single-leg, and tandem) on a firm surface followed by the same 3 stances in the same order executed on the foam pad (Alcan Airex, Sins, Switzerland). All stances are performed barefoot, each lasting 20 s with the participants' eyes closed and hands on hips. A trained rater counted the number of performance errors. Errors included lifting the hands off of the iliac crest; opening the eyes during the test; stepping, stumbling, or falling; moving the hip into more than 30° of flexion or abduction; lifting the forefoot or heel; or remaining out of the testing position for more than 5 s. The total numbers of errors were summed to determine the participant's score, with a higher score demonstrating poorer performance. The maximum number of errors for any single condition is capped at 10, or in total 60 maximum possible errors. An escalation from baseline in the number of errors greater than 3 within the 6 conditions indicated a possible concussion [16,17]. Intra-class correlation coefficients (ICCs) were used to establish reliability metrics. Three testers in a 3-day pilot study of healthy individuals (n = 8) established intra-rater (ICC = 0.93,0.98, 0.93) and inter-rater reliability (ICC = 0.74) for the total BESS. Test-retest reliability ICC was 0.96.

Near point convergence (NPC)

NPC measures the ability to view a target without double vision as it approaches one's nose. NPC was measured using the standardized push-up method [7,47]. Briefly, the participant was seated (wearing corrected lenses, if necessary), and the accommodation convergence ruler (Bernell Incorp. Mishawaka, IN) was placed underneath the nose. The participant fixated on a card with a line of 4 letters and was instructed to focus on the letter "F" on the top line (font 14 point) of the card as the experimenter moved the card towards the participant's face, only stopping once the participant reported that the letter appeared double. The measurement started from 25 cm away with the examiner moving the card 1.5–2.0 cm per second. The test concluded when the participant stated that the target appeared double, and that measurement was recorded from the ruler in centimeters. The previously reported cut-points for the NPC range from 5 cm to 17.5 cm; therefore, due to this variable range of cut points, the NPC cut point for the athletic population has yet to be determined [39]. Three testers in a 3-day pilot study of healthy individuals (n = 8) established intra-rater (ICC = 0.92, 0.89, 0.91) and inter-rater reliability (ICC = 0.96) for the near point convergence measures. Test-retest reliability ICC was 0.82.

Horizontal eye saccades (HES)

HES measures the participant's ability to quickly move the eyes back and forth between targets. To measure HES the participant was seated in front of a white sheet with 2 stationary targets (i.e., 2 x's in 48 bold, Arial font 25 cm apart at eye level and arm's length distance away). The participant was instructed to quickly look back and forth from one target to the next using only eye movements (without moving the head) synchronized with the sound of a metronome (Metronome, ONYX iPad App) beeping at 120 beats for 1 min (1 Hz = full cycle back and forth). The examiner watched the eyes for quickness, smoothness, and accurate fixation of the target. The dependent variables were three 7-point verbal rating scales (VRS) used to subjectively report dizziness, headache, and nausea ("No symptoms" = 0, the highest level of symptoms = 6). The within-subject change from baseline level was used for outcome measure analysis. Before and after the test, the participant was asked the level of each symptom separately (i.e., headache, dizziness, nausea) using the VRS. A previous report determined that the cutoff score for a positive test occurs when the patient reports an increase of 2 or more on the VRS [32]. Normal or abnormal (disconjugate eye movement, or over/undershooting the target) saccadic eye movement was visually observed by the examiner and recorded as either positive or negative (i.e., present or absent). There were no eye movements rated abnormal during pilot testing of healthy individuals; therefore, this ceiling effect resulted in all HES ICCs being equal to 1.0 during pilot testing.

Slow and fast smooth pursuit

Smooth pursuits were used to test the participant's ability to follow a slow- or fast-moving target with their eyes. The seated participant was instructed to focus on the tip of a pen held at eye level by the experimenter. The examiner stood approximately 1 m away and moved the pen horizontally 0.5 m to the left and right (~30° in each direction) to the beat of a metronome for 30 s. The participant was instructed to follow the target with their eyes only. The slow condition required participants to make a 30° smooth pursuit movement at 60 beats per minute for 30 s, which was followed by the fast pace condition at 100 beats per min for 30 s. The participant was asked their baseline level of dizziness, headache, and nausea using the VRS before testing, then again after both slow and fast smooth pursuit tests. A previous report determined that the cutoff score for a positive test occurs when the patient reports an increase of 2 or more on the VRS [32]. Normal or abnormal (disconjugate eye movement, or over/undershooting the target) saccadic eye movement was visually observed by the examiner and recorded as either positive or negative (i.e., present or absent). There were no eye movements rated abnormal during pilot testing of healthy individuals; therefore, this ceiling effect resulted in all smooth pursuit ICCs being equal to 1.0 during pilot testing.

Optokinetic stimulation (OKS)

OKS measures whether a normal reflexive optokinetic nystagmus (OKN) response is elicited when viewing a moving striped visual stimulus with whole or part of the visual field [8,48]. This test was performed using an OKN drum iPad app, which displays a high contrast grating passing horizontally across the visual field (OKN Stripes, downloadable app; Settings: red and white

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drum, 0.5 cm line width, 8.6 cm/s), which when held 15–20 cm from the eyes covers approximately a 60° diagonal field of view (FOV). Although both smooth pursuit and OKN will be activated by the stimulus used in this part of the study [22] our goal was to expose the participants to a fast moving optic flow field to elicit nystagmus, in general, and potentially induce S/S. To distinguish it from smooth pursuit test mentioned above, we refer to it nominally as OKS. The participant reported a baseline level of dizziness, headache, and nausea using the VRS. The seated participant was asked to maintain focus on the center of the iPad while the stripes were moving horizontally to the right for 30 s. This was immediately followed by a 30-s period of viewing the stripes moving horizontally to the left. After the full minute of OKS stimulation, the participant was asked to report levels of dizziness, headache, and nausea on the VRS before and after the test. Normal or abnormal (absence of normal fast phase nystagmus) optokinetic reflex was also assessed by observation. There were no eye movements rated abnormal during pilot testing of healthy individuals; therefore, this ceiling effect resulted in all OKS ICCs being equal to 1.0 during pilot testing.

Horizontal gaze stabilization test (GST)

The GST assesses the ability to stabilize vision as the head moves, which evaluates vestibular ocular reflex (VOR) function. The participant stood fixating a single visual target (i.e., an "X" on a piece of paper with Arial, bold, 48 font) at eye level, arm's length away. The participant was asked their level of dizziness, headache, and nausea using the VRS. They were instructed to turn their head horizontally approximately 30° in each direction to the beat of the metronome (240 beat per min) for 1 min. The participant was instructed to fixate their eyes on the target, and report if the target became blurry, or started to bounce around (i.e., oscillopsia). The participant was asked their baseline level of dizziness, headache, and nausea using the VRS before testing, then again after testing. A previous report determined that the cutoff score for a positive test occurs when the patient reports an increase of 2 or more on the VRS [32]. The quality of the VOR was also recorded as abnormal if the participant reported that the visual target was bouncing/blurry, or the experimenter noted excessive saccades in directions misaligned with the stimulus. There were no abnormal reflexes observed during pilot testing of healthy individuals; therefore, this ceiling effect resulted in all GST ICCs being equal to 1.0 during pilot testing.

Head thrust (VOR test)

The head thrust test evaluates the ability to stabilize vision as the head moves (i.e., VOR). The participant was seated and asked to fixate on the examiner's nose and to relax his or her head and neck as the examiner moved the participant's head quickly to the left or right. The examiner's hands were placed on the subject's occiput with thumbs on the temples rather than the temporomandibular joint. The examiner tilted the participant's head slightly down in order to provoke the horizontal semicircular canals (down about 30°). The head was first gently rotated to left and right ±45° to assess the participant's range of motion of neck and extra-ocular muscles. Then the head thrust was performed in the horizontal plane randomly to the right and left 3–4 times ±30°. The participant was asked their baseline level of dizziness, headache, and nausea using the VRS before and then again after VOR testing. Normal or abnormal VOR was also recorded. Abnormal VOR was recorded if the participant was unable to keep focused on the examiner's nose or the experimenter noted excessive saccades in directions misaligned with the stimulus. There were no abnormal reflexes detected during pilot testing of healthy individuals; therefore, this ceiling effect resulted in all VOR ICCs being equal to 1.0 during pilot testing.

Dynamic visual acuity (DVA)

The DVA test compares visual acuity when the head is static compared to when the head is moving to assess VOR function. A tumbling E visual chart was used to document visual acuity when the head was not moving. The participant stood 2.0 m from the chart per standard protocol and was asked to read the orientation of the E (i.e., left, right, up, or down) starting from the top until they could no longer read the chart clearly (i.e., no errors when reading the entire line). This was repeated while the participant actively moved his or her head 30° to left and right in the horizontal plane to the beat of the metronome (180 beats per min). The dependent variable is the line difference between the lowest line read with the head static and the head dynamic. Previous authors reported the cut-off points to be a loss of 3 or more lines during dynamic testing conditions is suggestive of potential vestibular dysfunction [20]. Three testers in a 3-day pilot study (n=8) established intra-rater (0.71, 0.84, 0.70) and inter-rater reliability (0.86) ICCs for the DVA test. Test-retest reliability ICC was 0.53. Due to these lower ICC values we re-examined the protocol and determined that the errors occurred in maintaining speed of the athlete's head as well as in what constitutes an incorrect line. After this re-examination this improved the raters' ability to use this test.

King-Devick (KD) tool

The KD tool is a test that requires control of oculomotor, attentional, and language processes. Suboptimal performance on this test has been shown to be a sensitive indicator for detecting injury due to concussion [12,13]. The KD utilizes 3 test cards with a series of a single-digit numbers that are read aloud from left to right as quickly as possible without making any errors. [12,13]. The test includes one demonstration card and 3 tests cards. The 3 tests cards were repeated a second time in the same order. The cumulative time taken for reading the 3 cards twice through was recorded for the KD score. The participants were instructed beforehand to correct any errors as quickly as possible. Errors were also summed together to arrive at a KD error score. The KD test has been found to have moderate test-retest reliability (ICC=0.70–0.78) [12,13]. In our pilot tests (n=8) with 3 testers across 3 days, ICCs for intra-rater (0.97,0.97, 0.96), inter-rater reliability (0.99), and test-retest (0.96) reliability were established.

Procedures

All participants performed the BESS and SOT protocols, in random counterbalanced order, and then proceeded to the vestibular and oculomotor assessment portion. Pilot testing of healthy individuals (n=8) prior to this experiment found no statistically significant order effects ($p=0.37$); however, some participants reported feeling less stable in the balance tests if the vestibular/oculomotor tests were performed first. Therefore, all participants in this experiment were tested on balance assessments first. The order of the vestibular and oculomotor assessments were NPC, HES, smooth pursuit tests, OKS, GST, head thrusts, DVAT, and KD test. All protocols were administered individually in a laboratory setting. The entire testing protocol took approximately 45 min to complete.

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Statistical methods

Group differences in demographics, SOT composite and BESS total scores were analyzed using independent sample 2-tailed t-tests. The SOT conditions and BESS test stances were each analyzed using a 2 (group)×6 (condition) repeated measures ANOVA. Violations of sphericity were checked by Mauchly's test, and in cases where a large violation of sphericity occurred a MANOVA was used [10]. Between-group differences in reporting a history of previous concussion were calculated with a chi-square test. Pearson's correlations between balance, vestibular, and oculomotor assessments were examined within healthy participants to determine concurrent validity. A logistic regression for binary outcomes ("Enter Method" and "Forward Conditional") was performed to examine predictive validity of the balance, vestibular, and oculomotor assessments. From the logistic regression classification table, "accuracy" was calculated as the sum of the true positives and true negatives divided by the total sample size. Positive predictive value (PPV) was calculated using the sum of the true positives divided by the total number of concussed individuals in the sample (n = 12). Logistic regression provided weighted coefficients (beta weights) for defining a regression model. The regression model was tested using receiver operating characteristic (ROC) curves. Then, area under the curve (AUC) for these ROC curves was calculated and a cutoff score was determined by choosing the value that maximized sensitivity and specificity. All statistical analyses were conducted using SPSS software (version 22.0; IBM Corporation, Armonk, NY) and significance was set at alpha equal to 0.05. Bonferroni correction was used to adjust *p*-values for multiple comparisons.

Results

Demographic data

Means and standard deviations between groups are reported in **Table 2**. There were no differences in sex, height, weight, or years of experience within their main sport between groups. The concussed and healthy groups differed in age by 1.5 years on average, which was statistically different ($p = 0.039$), but not clinically meaningful. The concussed participants performed the initial testing session on average 28 days post-injury (range 2–96 days). The concussed participants had significantly more previous concussions (2.6 concussions) compared to the controls (0.4 concussions; $p = 0.024$), where the concussed cohort in this study was 20 times more likely to report a history of concussion ($p \leq 0.001$). Raw data from the 12 concussed participants are reported in **Table 3**. Following the SOT and BESS tests, 2 of the participants with a concussion reported headaches, one reported just feeling dizzy, one reported both headache and dizziness, and one reported feeling headache, dizzy, and nauseated. All reported a 1–2 out of 6 (very mild S/S). 8 of the participants with a concussion reported no S/S at the start of the vestibular and oculomotor assessment.

Table 2 Descriptive characteristics of participants enrolled in study.

Variables	Concussed Participant n = 12 M ± SD	Healthy Participants n = 60 M ± SD	*p*
Age	21.7 ± 3.6	20.3 ± 1.8	0.039 *
Height	68.3 ± 3.7	69.4 ± 4.2	0.399
Weight	157.5 ± 26.8	160.6 ± 18.6	0.722
Years Experience	8.0 ± 5.7	10.5 ± 5.4	0.189
No. of Previous Concussions	2.6 ± 2.9	0.4 ± 0.8	0.024 *
Sex n (%)			0.629
Male	7 (58.3%)	35 (58.3%)	
Female	5 (41.7%)	25 (41.7%)	

M (mean), SD (standard deviation), n (number). * significance at $p < 0.05$

Balance assessments

The BESS test showed that the concussed group performed at or above the healthy group but there were no statistically significant differences between groups in the total score or in any individual stance conditions after correcting for multiple comparisons ($F_{5,66} = 1.82$, $p = 0.12$; **Table 4**). Logistic regression revealed that the BESS did not improve accuracy, moreover the sensitivity of the test was 8.3%, meaning only one in 12 of the individuals with concussion was correctly identified.

The SOT showed that the concussed group scored significantly lower on the SOT in the individual conditions ($F_{5,65} = 3.26$, $p = 0.011$), which were found to be due to differences in condition 3 ($p = 0.044$) and condition 4 ($p = 0.033$). The SOT visual ratio revealed that these difficulties were visually related ($p = 0.032$). Logistic regression revealed that the SOT had a sensitivity of 33.3% and a PPV of 66.7%.

Vestibular and oculomotor assessments

The mean NPC distance was trending toward statistical significance with the concussed group showing larger NPC measures compared to the control group ($p = 0.069$). The mean NPC distances in the concussed group (6.0 ± 4.1 cm) and the healthy control group (3.6 ± 2.2 cm; **Table 4**) correlated significantly with health status ($r = 0.337$, $p = 0.004$; **Table 5**). The DVAT test showed no significant differences between groups ($p = 0.592$; **Table 4**) and no correlation with health status ($r = 0.06$, $p = 0.592$; **Table 5**). The KD test completion time did not show a significant difference between the concussed and healthy groups ($p = 0.40$; **Table 5**) and did not correlate with health status ($r = 0.18$, $p = 0.129$; **Table 5**). The mean cumulative time for the concussed group was 90.0 ± 34.9 s, and the mean time for the healthy control group was 81.1 ± 13.1 s (**Table 4**).

Symptom provocation after vestibular and oculomotor assessments

There was a significant difference in OKS ($p = 0.033$) and GST ($p = 0.022$) S/S provocation reported between groups. The mean S/S reported for OKS and GST within the concussed group was 2 on average, whereas the healthy control group reported no S/S 94.6% of the time (**Table 4**). HES also had a mean S/S of 2 reported with a between-group difference trending towards significance ($p = 0.061$). Each of these assessments correlated significantly with health status ($p < 0.001$, **Table 5**).

Predicting concussed and healthy controls

A logistic regression model was found by testing the assessments, which were significantly correlated with concussion health status (**Table 5**). Those significantly correlated with health status were SOT condition 2 ($p = 0.036$), condition 3 ($p = 0.001$), condition 4 ($p = 0.033$), SOT visual ratio ($p = 0.032$) and visual preference ratio scores ($p = 0.028$), NPC ($p = 0.004$), OKS S/S score ($p < 0.001$), HES S/S score ($p < 0.001$), GST S/S score ($p < 0.001$). Using these assessments, we performed multivariate

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Table 3 Individual assessment scores, concussion group.

Subject	Days since injury	BESS	SOT	NPC	HES S/S				OKN S/S				GST S/S				DVA	KD
					Head-ache	Dizz	Nausea	Total	Head-ache	Dizz	Nausea	Total	Head-ache	Dizz	Nausea	Total		
1	2	17	83	6	0	0	0	0	0	0	0	0	0	0	0	0	1	33.3
2	4	14	78	3	1	0	0	1	1	0	0	1	1	0	0	1	1	42.5
3	8	2	87	1.5	1	1	0	2	1	0	0	2	2	1	0	3	1	43.2
4	8	3	84	9	0	0	0	0	0	0	0	0	0	0	0	0	1	42.4
5	9	18	81	4	0	0	0	0	0	0	0	0	0	0	0	0	1	43.9
6	10	17	86	3	0	0	0	0	0	0	0	1	0	0	0	0	2	37.1
7	11	10	82	12	0	0	0	0	0	0	0	0	0	0	0	0	1	34.5
8	16	8	76	12	3	3	3	9	4	4	2	10	4	4	2	10	5	47.1
9	37	9	79	9	3	0	0	3	3	0	0	3	3	0	0	3	1	40
10	58	16	63	0	0	2	0	2	0	2	0	2	2	3	0	5	1	48.8
11	77	9	67	3.5	0	0	0	0	0	0	1	1	0	0	1	1	4	30.1
12	96	13	60	9	2	3.5	2	7.5	2	1	1	4	0	5	0	5	2	97.5

BESS (Balance Error Scoring System, total score), DVA (dynamic visual acuity, line difference), GST (gaze stabilization test), HES (horizontal eye saccades), KD (King-Devick, average of 2 trials), NPC (near point convergence), OKN (optokinetic reflex), SOT (sensory organization test, composite score), S/S (signs and symptoms)

Table 4 Means and standard deviations of concussion assessment scores.

Variables	Concussed Participant n = 12 M ± SD	Healthy Participants n = 60 M ± SD	*p*
BESS			
Total	11.8 ± 4.8	13.4 ± 4.5	0.230
Double Leg Firm	0.0 ± 0.0	0.0 ± 0.0	n/a
Single Leg Firm	1.7 ± 1.4	2.4 ± 1.9	0.172
Tandem Leg Firm	0.8 ± 1.0	1.1 ± 1.4	0.503
Double Leg Foam	0.1 ± 0.3	0.0 ± 0.1	0.448
Single Leg Foam	4.9 ± 1.6	6.2 ± 1.8	0.031
Tandem Leg Foam	4.2 ± 2.6	3.2 ± 1.5	0.570
SOT			
Composite	76.1 ± 8.5	79.6 ± 5.5	0.187
Condition 1	95.0 ± 1.3	95.3 ± 1.6	0.498
Condition 2	90.6 ± 5.5	92.8 ± 2.5	0.206
Condition 3	87.8 ± 5.9	91.7 ± 3.0	0.044 *
Condition 4	80.0 ± 10.1	86.0 ± 8.4	0.033 *
Condition 5	66.0 ± 10.2	68.0 ± 8.4	0.457
Condition 6	62.9 ± 15.6	67.0 ± 10.1	0.257
SOM Ratio	0.95 ± 0.5	0.97 ± 0.2	0.209
VIS Ratio	0.84 ± 0.1	0.90 ± 0.1	0.032 *
VEST Ratio	0.69 ± 0.1	0.71 ± 0.8	0.485
PREF Ratio	0.94 ± 0.7	0.97 ± 0.3	0.207
Vestibular and Oculomotor Assessments			
NPC	6.0 ± 4.1	3.6 ± 2.2	0.069
HES S/S score	2.0 ± 3.11	0.1 ± 0.3	0.061
Smooth Pursuit S/S	0.0 ± 0.0	0.0 ± 0.0	n/a
OKS S/S score	2.0 ± 2.8	0.0 ± 0.1	0.033 *
GST S/S score	1.9 ± 2.2	0.3 ± 0.7	0.022 *
DVA line difference	1.8 ± 1.4	1.5 ± 1.5	0.592
KD Score	90.0 ± 34.9	81.1 ± 13.1	0.400

M (mean), SD (standard deviation), n (number). BESS (Balance Error Scoring System), SOT (sensory organization test), SOM (somatosensory), VIS (visual), VEST (vestibular), PREF (visual preference), NPC (near point convergence), HES (horizontal eye saccades), OKS (optokinetic stimulation), GST (gaze stabilization test), DVA (dynamic visual acuity), KD (King-Devick), S/S (signs and symptoms). * BESS exam significance at $p < 0.025$ (0.05/2), * SOT exam significance at $p < 0.05$, * Vestibular and Ocular Motor exam significance at $p < 0.05$

Table 5 Correlation of concussion assessments with health status.

Variables	*r*	*p*
SOT		
Composite	−0.22	0.067
Condition 1	−0.08	0.498
Condition 2	−0.25	0.036 *
Condition 3	−0.38	0.001 *
Condition 4	−0.25	0.033 *
Condition 5	−0.09	0.457
Condition 6	−0.14	0.257
SOM Ratio	−0.26	0.028 *
VIS Ratio	−0.26	0.032 *
VEST Ratio	−0.08	0.485
PREF Ratio	−0.15	0.206
BESS		
Total BESS Test	−0.13	0.264
Double Leg Firm	n/a	n/a
Single Leg Firm	−0.16	0.172
Tandem Leg Firm	−0.08	0.503
Double Leg Foam	0.15	0.205
Single Leg Foam	−0.26	0.031 *
Tandem Leg Foam	0.10	0.409
Vestibular and Oculomotor Assessments		
NPC	0.34	0.004 *
HES S/S Score	0.49	< 0.001 *
OKS S/S Score	0.55	< 0.001 *
GST S/S Score	0.51	< 0.001 *
DVA Line Difference	0.06	0.592
KD Score	0.18	0.129

M (mean), SD (standard deviation), n (number). BESS (balance error scoring system), SOT (sensory organization test), SOM (somatosensory), VIS (visual), VEST (vestibular), PREF (visual preference), NPC (near point convergence), HES (horizontal eye saccades), OKS (optokinetic stimulation), GST (gaze stabilization test), DVA (dynamic visual acuity), KD (King-Devick), S/S (signs and symptoms). * significance at $p < 0.05$

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logistic regression for binary outcomes using the "Enter" method (**Table 6,7**), which provided the beta weights used to perform an ROC curve analysis. The regression equation with the greatest discriminant accuracy was

$$y_i = \beta_0 + \beta_{NPC} * (NPC)_i + \beta_{OKS} * (OKS)_i + \beta_{Som} * (Som)_i + \beta_{Vis} * (Vis)_i + \beta_{Vest} * (Vest)_i + \beta_{Pref} * (Pref)_i$$

This analysis identified the best subset of independent predictors of concussion as the 4 SOT sensory ratio scores (*SS* – somatosensory ratio, *Vis* – visual ratio, *Vest* – vestibular ratio, *Pref* – visual preference ratio), NPC, and OKS S/S score (accuracy = 98.6%, AUC = 0.983, $p \leq 0.001$). Although a similar model using the individual SOT conditions 2, 3, and 4 together with vestibular and oculomotor assessments was also highly accurate, these tended to result in over-fitting when applied all together. SOT visual preference ratio score, GST and HES could also be left out of the best model with little or no loss to accuracy. ROC curve analyses of each SOT sensory ratio individually revealed that only the visual ratio was a significant discriminator (AUC = 0.71, $p = 0.025$) with a sensitivity of 83% and specificity of 56% (**Table 8**). A second model without any SOT variables included using only OKS, GST, and NPC was still able to discriminate between groups accurately (accuracy = 94.4%, AUC = 0.951, $p \leq 0.001$). Individual evaluation of the vestibular and oculomotor assessments showed that the GST S/S score alone (accuracy = 87.5%, AUC = 0.74, $p = 0.008$) and OKS S/S alone (accuracy = 93.0%, AUC = 0.83, $p \leq 0.001$) were significant, but the NPC distance when used alone was not ($p = 0.125$). However, when NPC was combined with the other 3 assessments it significantly improved discrimination. In fact, when performing a forward, conditional logistic regression on all variables, the top 2 models were OKS S/S alone and OKS S/S plus NPC (accuracy = 93.0%) with the latter having a better ROC outcome (AUC = 0.94, $p \leq 0.001$).

Table 6 Concussion assessment model – binary logistic regression results.

Variables	ß	SE	Wald X^2	p
SOT ratios/OKS/NPC Model				
SOM Ratio	40.8	48.0	0.7	0.395
VIS Ratio	−25.0	11.2	5.0	0.026 *
VEST Ratio	47.4	22.7	4.4	0.037 *
PREF Ratio	12.7	18.6	0.5	0.495
NPC	1.1	0.5	5.4	0.020 *
OKS S/S Score	11.9	4.6	6.7	0.010 *
Constant	−76.9	56.4	1.9	0.173
Vestibular/Oculomotor Model				
NPC	0.6	0.3 6.2	0.013 *	
OKS S/S Score	120.4	10 339.0	0.0	0.991
GST S/S Score	−43.9	3 909.8	0.0	0.991
Constant	−5.9	1.7	12.0	0.001 *
OKS + NPC Model				
NPC	0.6	0.2	6.4	0.012 *
OKS S/S Score	5.0	1.4	12.1	0.001 *
Constant	−5.8	1.6	13.1	0.001 *

SE (standard error), CI (confidence interval), SOT (sensory organization test), SOM (somatosensory), VIS (visual), VEST (vestibular), PREF (visual preference), NPC (near point convergence), OKS (optokinetic stimulation), GST (gaze stabilization test), S/S (sign and symptom). * significance at $p < 0.05$

Discussion

The findings of this study demonstrate that using a condensed set of balance, and vestibular and oculomotor tests results in a model with the greatest accuracy for detecting concussion within the cohort tested. From the full battery of assessments that were tested in this study, the evidence supports using the SOT's ratio scores together with the NPC and the OKS S/S score to

Table 7 Logistic regression classification tables.

		SOT ratios/OKS/NPC Model Prediction		
		Health Status		Percentage Correct
Actual State		Healthy	Concussed	
Health Status	Healthy	59	0	100.0
	Concussed	1	11	91.7
Overall Percentage (Accuracy)				98.6
		OKS/NPC/GST Model Prediction		
		Health Status		Percentage Correct
Actual State		Healthy	Concussed	
Health Status	Healthy	58	1	98.3
	Concussed	3	9	75.0
Overall Percentage (Accuracy)				94.4
		OKS/NPC Model Prediction		
		Health Status		Percentage Correct
Actual State		Healthy	Concussed	
Health Status	Healthy	57	2	96.6
	Concussed	3	9	75.0
Overall Percentage (Accuracy)				93.0
		OKS Model Prediction		
		Health Status		Percentage Correct
Actual State		Healthy	Concussed	
Health Status	Healthy	58	1	98.3
	Concussed	4	8	66.7
Overall Percentage (Accuracy)				93.0

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get the highest sensitivity and specificity for discriminating individuals with concussion (subacute to chronic) from healthy controls. Even without the SOT ratio our preliminary results show that a brief 3-min test using only the NPC, OKS S/S, and GST S/S were able to discriminate health status with a sensitivity of 91.7% and specificity of 81.7%. Not only did sensitivity/specificity decrease when the BESS, SOT, and all of the vestibular and oculomotor measurements were included in the assessment model, but the full exam took approximately 45 min, which can be cumbersome to an athletic trainer as well as overwhelming to an athlete who has just sustained an injury.

Previous researchers have reported the SOT and BESS tests as reliable measures of postural control during concussion assessment. While some studies have found the SOT to have moderate reliability (ICC = 0.64–0.66) [16,51] another study looking individually at each condition found low to moderate reliability (ICC = 0.26–0.68, respectively) [11]. Very little research has been done to validate the SOT sensory ratios as a clinical marker for concussion [33]. The BESS test has been shown to have moderate to good reliability (ICC < 0.75) with moderate to high criterion-related validity depending on the stance assessed (r = 0.79 single foam, r = 0.64 tandem foam, r = 0.42 single leg firm, r = 0.31 double leg foam) [3]. Our findings indicate that the BESS test was unable to distinguish concussed from healthy athletes (r = −0.13), which may be due, in part, to our concussion population, since less than half were in the acute stage and none were within 48 h of injury. This is consistent with previous research, where the BESS test has been found to be the most sensitive when the athletes are tested during the acute stage [16,17].

Unlike the BESS, the SOT did show good sensitivity and specificity for detecting concussion in our sample. Previous research demonstrates that the Neurocom's SOT can be a good tool to assess deficiencies in the visual, vestibular, and somatosensory systems that may exist following a concussion even during the subacute stage [42]. There are subtle deficits to postural stability in participants with a history of concussion compared to those with no history of concussion, but others have found that these changes were not clinically significant [42]. Our results are in agreement with this, in that concussed athletes even in the subacute concussion stage score worse on the SOT; however, the differences in the SOT individual conditions and composite scores between groups were not large enough to establish a clinical cut point. Moreover, our results demonstrate that the SOT sensory ratios may be more clinically relevant than the composite and individual condition scores on the SOT.

Oculomotor assessments that have previously been found to be sensitive to concussion include static and dynamic vergence [44]. A recent study found that measuring NPC increased the probability of accurately diagnosing a concussion by at least 34% [32]. In the current study, we also found that measuring NPC adds to the sensitivity and specificity when using a cut point of 4 cm. Our NPC mean is within the range of what other studies report [7,32,47]; however, more research is necessary for determining a cut-point for a concussed athlete. Another oculomotor assessment relied on assessing the optokinetic reflex and measuring S/S following OKS. There is only sparse literature showing the use of OKS on concussed athletes; however, a recent case study on one patient with PCS showed that gradual habituation to OKS together with balance training helped significantly reduce chronic symptoms [35]. Our study found OKS to be the most sensitive measure for discriminating concussed from healthy individuals. By itself, it was found to have a highly significant AUC (**Table 8**), and when combined with other assessments, concussion detection was nearly perfect. This is encouraging evidence since this simple yet sensitive test can easily be added to a multifaceted battery of concussion assessments. One caveat that should be noted is that we used an optic flow field that covered only a 60° diagonal FOV, which may have elicited a combination of OKS and smooth pursuit [22]. Though dissociating these 2 oculomotor processes may be important for uncovering the underlying etiology of post-concussive symptoms, for the purposes of clinical assessment using less than a full FOV visual stimulus still proved to be a very sensitive tool. In future investigations, a full FOV stimulus may demonstrate even greater sensitivity and allow us to further describe the root of the oculomotor deficits associated with concussion.

Other oculomotor assessments that have been found to be reliable measures for assessing concussion in athletes were not found to be good discriminators in the current study. For example, the KD test has also been shown to correlate with post-concussion signs and symptoms score [45], but in a heterogeneous subacute cohort of individuals with concussion as was tested in this study, it was neither sensitive nor specific, and did not contribute significantly to our concussion detection model. Similarly, the DVAT, which has been shown to have moderate reliability using a computerized version of the test [24,38,49], did not discriminate between groups in the cohort we tested. A contributing factor to this lack of sensitivity may be due to great variation in how this test is applied across research studies, which reveal that no consensus in protocol has been reached (e.g., with or without computerized head tracking, velocity of head movements, angle of head movement, active vs. passive head movement) [24,38,49].

There has been a paucity of research examining VOR assessments in concussed athletes, however there is evidence that VOR abnormalities are prevalent following mild head trauma [2,21]. The GST, which is a valid measure of VOR dysfunction [15], has been found to have moderate reliability to identify vestibular ocular deficits in individuals with concussion-like injury due to whiplash [46]. In a study that specifically focused on concussed athletes [32], GST together with oculomotor assessment of repetitive volitional eye saccades (i.e., HES) were tested, revealing that eye and head movements in the horizontal plane were the most sensitive [32]. Additionally, if the athlete reported at least 2 or more S/S on one of these tests, this increased the probability that the individual has suffered a concussion by at least 46% [32]. Our results were similar in that our concussed athletes on average reported 2 or more S/S following the GST, OKS, and HES; however, only the GST and OKS were significant predictors

Table 8 ROC scores for SOT ratios, OKS S/S, and NPC individually.

Test	AUC	Cut-Point	p
SOM Ratio	0.611	0.97	0.228
VIS Ratio	0.707	0.91	0.025 *
VEST Ratio	0.538	0.09	0.095
PREF Ratio	0.578	0.71	0.339
NPC	0.641	3.95	0.125
OKS S/S score	0.828	0.50	0.000 *
GST S/S score	0.743	0.50	0.008 *

AUC (area under the curve), SOT (sensory organization test), SOM (somatosensory), VIS (visual), VEST (vestibular), PREF (visual preference), NPC (near point convergence), OKS (optokinetic stimulation), GST (gaze stabilization test), S/S (signs and symptoms). * significance at $p < 0.05$

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of concussion. Our ROC curve analysis suggests that any increase in GST beyond baseline scores could be indicative of a concussion. However, the vestibular assessment was much stronger when combined with an oculomotor assessment (e.g., OKS or NPC).

Finally, several variables have been identified as risk factors for prolonged concussion recovery in other studies. For example, previous history and number of concussions, as well as specific S/S at the time of injury (e.g., headaches, dizziness) [6,25,26,37] predispose an athlete to prolonged recovery following concussive injuries. Out of all the risk factors, history of concussive injuries has the longest known association with increased concussion susceptibility [40]. One study found that football athletes with a history of concussions are more likely to take greater than 7 days to recover [29] and there is a 2.0–5.8 times greater risk of sustaining another concussion [37]. Despite this evidence, an association between concussion history and rate of recovery is still debatable. Lau et al. reported no difference in history of concussions and time of recovery [26], while others have identified significant differences between recovery rates of neurological function after a second concussion [41]. Another study found that only post-concussion S/S scores predicted recovery, whereas concussion history and loss of consciousness were not predictors for recovery duration [31]. Although our study was not designed at the outset to systematically investigate the role of concussion history, a cursory analysis that grouped all participants with a history of previous concussions (n = 17) and compared them to those with no history of concussion (n = 55) showed that SOT, NPC, OKS S/S, GST S/S were all sensitive to this group variable ($p < 0.05$, Student's t-tests). Further investigation is required, however these results support the notion that concussion history may contribute to risk of future injury. Athletes may have lingering subacute symptoms affecting balance and sensorimotor control, which degrade performance and could expose a player to new injury after returning to play.

There were several limitations that should be noted. First, although our normative baseline for the healthy controls is a moderately large sample at n = 60, our sample of concussed individuals includes only 12 participants. Despite the fact that the concussed sample size is small, we were still able to detect differences in many of the SOT and vestibular and oculomotor assessments. Another limitation of this study is that we do not have a homogenous concussed population. Only half of the subjects fell within the acute period (< 2 weeks), while the rest were greater than 3 weeks post-injury and were possibly suffering from post-concussive syndrome. Interestingly though, despite the chronic state of many of our concussed participants, our assessment approach was still highly accurate. Future research will need to validate these findings in a larger cohort with a clearly defined concussed group, which can be stratified into acute vs. chronic groups or analyzed with time since injury as a covariate. Lastly, the vestibular oculomotor assessments are still based largely on participant reports of signs and symptoms provocation, which relies on the accuracy and integrity of subjective report. Therefore, ensuring subjective measures are supplemented by objective measures, which may include a neurocognitive exam, would all serve to provide a more comprehensive multi-faceted approach to concussion assessment.

Conclusion

These preliminary findings suggest that using this condensed exam consisting of the OKS S/S, NPC, and GST S/S is a valid measure for discriminating athletes impaired by concussion in the subacute stage from healthy controls, and eliminates the time-consuming burden of performing all of the balance, vestibular, and oculomotor tests available to athletic trainers.

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Appendix 6

Title: “Visual-vestibular processing deficits in mild traumatic brain injury”

Wright WG[1,2,*], Tierney RT[3], McDevitt J[1,4]

[1]Department of Physical Therapy, Temple University, Philadelphia, PA USA
[2]Department of Bioengineering, Temple University, Philadelphia, PA USA
[3]Department of Kinesiology, Temple University, Philadelphia, PA USA
[4]Department of Athletic Training, East Stroudsburg University, East Stroudsburg, PA USA

*Corresponding author:
W. Geoffrey Wright, PhD
wrightw@temple.edu

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Abstract
BACKGROUND: The search for reliable and valid signs and symptoms of mild traumatic brain injury (mTBI) has lead to a growing body of evidence that individuals with long-lasting, unremitting impairments often experience visual and vestibular symptoms, such as dizziness, postural and gait disturbances. In this study we evaluate the role of visual-vestibular processing deficits following mTBI.
METHODS: A number of clinically accepted vestibular, oculomotor, and balance assessments as well as a novel virtual reality (VR)-based balance assessment device were used to assess adults with concussion (n=14) in comparison to a healthy age-matched cohort (n=58). **RESULTS**: Significant between-group differences were found with the VR-based balance device (p=0.001), with dynamic visual motion emerging as the most discriminating balance condition. The symptom reports collected after performing the oculomotor and vestibular tests: rapid alternating horizontal eye saccades, optokinetic stimulation, and gaze stabilization, were all sensitive to health status ($p<0.05$), despite no oculomotor abnormalities being observed except for near-point convergence. The BESS, King-Devick, and Dynamic Visual Acuity tests did not detect between-group differences.
CONCLUSION: Postural and visual-vestibular tasks most closely linked to spatial and self-motion perception had the greatest discriminatory outcomes. The current findings suggest that mesencephalic and parieto-occipital centers and pathways may be involved in mTBI.

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1. Introduction

Determining whether an individual has suffered a concussion often requires the employment of many clinical assessments including cognitive, psychological, motor, balance and gait tests, as well as a self-report of symptoms [15, 20, 25, 38]. Although concussions, also referred to as mild traumatic brain injury (mTBI), are commonly reported to resolve within 7-10 days, there are currently no objective measures for diagnosing concussion, instead it is identified by functional deficits and clinical judgment [38]. Therefore, the accuracy of the clinical diagnosis is largely dependent on the sensitivity and specificity of the tests used to detect signs and symptoms (s/s), rather than being able to detect and identify structural deficits. In the acute stage of concussion (<7 days), many of the clinical assessments have been shown to be highly sensitive to symptom detection. Beyond a few days post-injury sensitivity tapers off significantly, which may lead to a premature diagnosis of "good health". This occurs in part because secondary injuries follow a delayed timeline in a cascade of biochemical, molecular and physiological events at the cellular level that are triggered by the primary mechanically-induced injury [21]. Detecting physical evidence of diffuse axonal damage from the primary injury or cellular damage from the secondary injuries has not yet reached a high level of diagnostic precision, therefore an effective approach for patient management continues to involve symptomatology.

The search for reliable and valid s/s of concussion has lead to a growing body of evidence that individuals with long-lasting, unremitting impairments often report vestibular symptoms, such as dizziness, and postural and gait disturbance [1, 2, 4, 28]. In fact, dizziness is reported in over 50% of concussions and is associated with a greater than a six-fold increased risk for prolonged recovery [34]. Other related symptoms include sensitivity to visual motion, which can also persist beyond the acute period [8, 10, 29, 39, 43, 56]. Furthermore, there is a well-established body of research that shows oculomotor function can be impaired [13, 26, 40, 47], which affects not only visual control, but postural stability as well.

Postural assessment is recommended in the Zurich Consensus Statement [38]. Common tests include the Balance Error Scoring System (BESS) or Neurocom's Sensory Organization Test (SOT, Natus Medical, Inc. [42]), both of which have been shown to be sensitive to postural deficits during the first few days after injury [5, 11, 23, 37, 44]. While the BESS and SOT tend to be most sensitive in the very acute stage of recovery [22, 37], many studies now suggest there are postural and motor symptoms that do not spontaneously resolve with a week or two [4, 28]. New balance measures that are proving to be sensitive beyond the acute stage involve virtual reality (VR) technology [43, 45, 47, 55]. Balance assessment using VR has been applied to other clinical populations with visual and/or vestibular processing issues [30, 32] and is now becoming more common in TBI assessment. These measures have been found to be not only reliable and valid in detecting concussion symptoms, but exposure to dynamic motion in VR during balance and gait challenges has also been found to be beneficial in treatment of post-concussive dizziness and postural dysfunction [43]. These findings may suggest that the inherent visual-vestibular conflict that virtual reality creates [52, 54] enhances the sensitivity of the VR approach to detect balance deficits lasting into the later stages of mTBI recovery.

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The link between visual and vestibular motion processing is an integral part of spatial orientation perception and balance control. The vestibular and oculomotor systems are important for sensing angular and linear acceleration of the head and eyes, which enables a moving individual to maintain gaze on a stable target or a stationary individual to focus on a moving target. Assessing peripheral vestibular, visual, oculomotor function together with balance and gait is a necessary approach to understanding how these processes influence one another, especially when one or more is damaged. Their covariance likely plays a role in why they have all been found to be sensitive to brain injury. Despite the growing number of studies that are being done to examine the multifactorial combination of sequelae following mTBI [2, 15, 26, 40], there is no consensus criterion-measure for assessing whether an individual's symptoms have fully resolved. Combining visual and oculomotor assessments with others that examine whole-body behavioral output of vestibular, visual, and somatosensory integration (e.g., postural balance) may provide comprehensive information and greatly improve concussion management. The purpose of this study was to evaluate the role of visual and vestibular processing deficits following mTBI in the acute to subacute stages of recovery. This study compares a number of common vestibular, oculomotor, and balance assessments as well as a novel balance assessment device that uses virtual reality visual stimulation to challenge visual-vestibular processing in persons with and without mTBI.

2. Methods

Subjects

All individuals with concussion (n=14) were evaluated by a certified athletic trainer or physical therapist during the initial evaluation. All individuals with concussion reported that they had experienced a head impact in addition to having experienced concussion s/s, and performed the initial testing session within four months post injury (mean = 36 days; range 2 - 120 days; n=2 acute, <7 days post-injury, n=12 subacute, >7 days post-injury). The healthy individuals (n=58) were included if they reported no concussion within the last six months; only three healthy participants had any history of concussion (Concussion cohort = 3.5 vs. Healthy cohort = 0.14 lifetime concussions, p = 0.001). The ages and gender distribution did not differ between groups. All subjects signed a Temple University IRB-approved consent form in accordance with the guidelines of the Helsinki Accords. All subjects received monetary compensation for participation in the study.

Protocol

All participants performed a series of balance, vestibular, and oculomotor assessments, which have been previously described in greater detail [39, 56]. Subjective reports of symptoms were collected before and after the vestibular and oculomotor assessments noted below. Although the experimenter also assessed the saccades and head movements in each of these test for quickness, smoothness, and/or accurate fixation of the target, only the verbal rating scales (VRS) symptoms are reported here. Our previous study has shown that clinical assessment of behavioral signs were less sensitive than the subjectively reported symptoms [39]. The VRS consists of three 7-point scales, which are subjective reports of dizziness, headache, and nausea ("No symptoms" = 0, the highest level of symptoms = 6). The within-subject change from baseline level was used for

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outcome measure analysis. Before and after the test, the participant was asked the level of each symptom separately. The cutoff score for a positive test occurs when the participant reports an increase of two or more on the VRS [40].

Balance assessments

Virtual reality (VR)-based balance device – this new portable postural assessment device uses custom-designed software and commercially available technology (i.e. Wii Balance Board [WBB], 60" television, Bluetooth USB, desktop computer). It has previously been shown to be reliable and valid for postural assessment [56]. Our visual stimulus uses a high-resolution digital snapshot taken of an immersive VR scene, which depicts a three dimensional environment of an outdoor temple with Greek columns, marble flooring, Persian rugs and a mountain range in the distance (VRCO, Virginia Beach, VA, [31]). The VR scene is passively rotated about the subject's roll axis at 60º/s in the dynamic visual conditions, which was chosen because visual motion about the roll axis has been shown to be posturally destabilizing, especially at velocities >25º/s [16, 31, 42]. Moreover, concussed and sub-concussed populations have been found to be more sensitive to visual roll tilt than other axes of visual tilt [24, 45, 46]. Center-of-pressure (COP) time series data is collected at 100hz, and from that COP sway area, sway velocity, and standard deviation in anterior-posterior (AP) direction and the mediolateral (ML) direction are derived. Six balance conditions are collected in the dark with barefoot participants standing 40 cm from the television screen in a completely dark room. The six conditions are (1) EO-Firm: Eyes open while standing on a firm and stable support surface while viewing a static visual scene, (2) EC-Firm: Eyes closed while standing on a firm and stable support surface and dark screen, (3) DYN-Firm: Eyes open while standing on a firm and stable support surface while viewing a dynamically rotating scene, (4) EO-Foam: Eyes open while standing on a unstable support (Airex foam pad placed on top of the WBB) and stable visual scene, (5) EC-Foam: Eyes closed on foam support, and (6) DYN-Foam: Eyes open while standing on an unstable foam support while viewing a dynamically rotating scene.

Balance Error Scoring System (BESS) - this test provides a measure of postural stability by subjectively counting errors during a series of six balancing stances [22]. All postural conditions are tested in bare feet with eyes closed. The six conditions, always tested in the same order, are three stances (double-leg, single-leg, and tandem) on a firm surface followed by the same three stances in the same order executed on the foam pad (Alcan Airex, Sins, Switzerland). A trained rater counted the number of performance errors. The total numbers of errors were summed to determine the participant's score, with a higher score demonstrating poorer performance.

Oculomotor tests

Rapid Horizontal Eye Saccades (HES) - this test measures the participant's ability to quickly saccade left and right between targets. A seated participant is instructed to quickly look back and forth from one target to the next using only eye movements (without moving the head) synchronized with the sound of a metronome (Metronome, ONYX iPad App) beeping at 120 beats for 1 minute (1 Hz = full cycle back and forth). The participant was asked to report s/s before and after this test.

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Fast Smooth Pursuit - smooth pursuit tasks were used to test the participant's ability to follow a fast moving target with their eyes. The seated participant was instructed to focus on the tip of a pen held at eye level by the experimenter while it was moved horizontally 0.5 m to the left and right (~30º in each direction) to the beat of a metronome (100 beats per minute) for 30 sec. The participant was instructed to follow the target with their eyes only. Abnormal eye movements were recorded if the participant was unable to keep focusing on the pen tip or the experimenter noted excessive saccades in directions misaligned with the stimulus.

Optokinetic stimulation (OKS) - a normal reflexive optokinetic nystagmus (OKN) response is elicited when viewing a moving striped visual stimulus with whole or part of the visual field [14, 47]. The participant was asked to report s/s before and after this test.

Near Point Convergence (NPC) – this test measures the ability to adduct and accommodate the eyes to view a target without double vision as it approaches one's nose. NPC was measured using the standardized push-up method [12, 38].

King-Devick (KD) Test – this test evaluates oculomotor, attentional, and language processing involving a series of single-digit numbers that are read out loud as quickly and error-free as possible. The test has been shown to be sensitive to detecting brain injury symptoms [19]. The cumulative time taken for reading the three cards twice through is recorded as the total KD time. Error-rate did not differ between groups, so is not included in further analyses.

Vestibular tests

Dynamic Visual Acuity Test (DVAT) – this test compares visual acuity when the head is static compared to when the head is moving to assess VOR function [35]. The dependent variable is the line difference between the lowest line read with head static and head dynamic.

Horizontal Gaze Stabilization Test (GST) – the GST assesses vestibular ocular reflex (VOR) by testing an individual's ability to stabilize vision on a visual target as the head is actively nodded repetitively in the left-right direction. The participant was asked to report s/s before and after this test.

Head Thrust (VOR test) – this test evaluates VOR by assessing the ability to stabilize vision as the head moves. The participant was seated and asked to relax his/her head and neck as the experimenter moved the participant's head quickly to the left or right while fixating the experimenter's nose. The head thrust was performed in the horizontal plane randomly to the right and left three to four times ±30º. Abnormal VOR was recorded if the participant was unable to keep focused on the examiner's nose or the experimenter noted excessive saccades in directions misaligned with the stimulus.

Statistical Methods

A 2 (group) x 2 (surface) x 3 (visual condition) repeated-measures ANOVA was used to analyze any significant main or interaction effects. Due to large differences in group samples, violations of sphericity were checked by Mauchly's test, and in cases where a large violation of sphericity occurred a MANOVA was used [18]. Between-group proportional differences in reporting a history of previous concussion was calculated with a chi-square test. Pearson's correlations between balance, vestibular, oculomotor assessments, and symptom reports were examined to determine which

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variables were correlated. Student's t-test for independent groups was used to analyze s/s with adjustments to degrees of freedom when Levene's test for equality of variances was significant. A logistic regression for binary outcomes ("Enter Method" and "Forward Conditional") was performed to examine predictive validity of the balance, vestibular, and oculomotor assessments. From the logistic regression classification table, "accuracy" was calculated as the sum of the true positives and true negatives divided by the total sample size. Logistic regression provided weighted coefficients (beta weights) for defining a regression model. The regression model was tested using receiver operating characteristic (ROC) curves. Then, area under the curve (AUC) for these ROC curves was calculated and a cutoff score was determined by choosing the value that maximized sensitivity and specificity. All statistical analyses were conducted using SPSS software (version 22.0; IBM Corporation, Armonk, NY) and significance was set at alpha equal to 0.05. Bonferroni correction was used to adjust *p*-values for multiple comparisons where applicable.

3. Results

Between-group comparisons

Balance data collected using the novel VR-based balance device showed a main effect of health status ($F_{1,69}$ = 12.5, p=0.001) with the concussed group showing greater COP sway area than the healthy group in all balance conditions. COP standard deviation in the ML ($F_{1,69}$ = 5.27, p=0.025) and AP ($F_{1,69}$ = 6.18, p=0.015) directions also showed a between group difference. COP sway velocity was not sensitive to health status (p=0.57).

Significant differences were found for all symptoms scores collected following oculomotor and vestibular tests: rapid alternating horizontal eye saccades (t(13.1) = -2.16, *p =0.05*, Student's t-test for independent samples), optokinetic stimulation (t(13.0) = -2.35, p = 0.035), and the horizontal gaze stabilization test (t(13.7) = -2.44, *p = 0.029*). The NPC sign also showed a significant between-group difference (t(14.7) = -2.66, *p = 0.018*).

Balance data collected from the BESS test showed no between-group differences for the total score (t(70) = 1.27, p = 0.21), nor did KD total time (t(70) = -1.55, p = 0.13) or the DVAT score (t(70) = -1.11, p = 0.27).

Correlation between assessments (see Table 2)

Health status correlated significantly with all six balance conditions. The highest r-values were for the two dynamic visual conditions (DYN-Firm*: r=0.33, p=0.005*; DYN-Foam: *r=0.42, p<0.001*). All s/s scores following the vestibular and oculomotor tests including the rapid alternating horizontal saccades (*r=0.46, p<0.001*), optokinetic stimulation (*r=0.50, p<0.001*), and the horizontal gaze stabilization test (*r=0.45, p<0.001*) were significantly correlated with health status. The near-point convergence distance was also significantly correlated with health status (*r=0.42, p<0.001*). However, the KD total time (*r=0.18, p=0.13, n.s.*), DVAT line difference (*r=0.13, p*=0.27, *n.s.*), and total BESS score (*r=-0.15, p*=0.21, *n.s.*) were not. There was no variability in the VOR head thrust or the smooth pursuit since all participants, healthy and concussed, were assessed to have normal response.

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Performance on the VR-balance test correlated most significantly with the symptoms scores following the gaze stabilization test (r_{max}*=0.55, p<0.001*), the optokinetic stimulation (r_{max}*=0.40, p*<0.001) and the rapid alternating horizontal eye saccades (r_{max}*=0.41, p*<0.001), but did not significantly correlate with any of the objective measures of oculomotor or vestibular function, including near-point convergence distance (r_{max}*=-0.14, p=0.24, n.s.*), KD total time (r_{max}*=0.17, p=0.16, n.s.*), DVAT line difference (r_{max}*=0.12, p=0.34, n.s.*), and total BESS score (r_{max}*=0.15, p=0.22, n.s.).*

Models from known-group analyses

For the VR-based balance conditions, COP sway area was analyzed using binary logistic regression because it had the highest between-group effects sizes relative to the other COP metrics. The regression model which included all six postural conditions had the greatest accuracy (87.5%) in classifying health status. A forward conditional logistic regression revealed that the DYN-Foam condition by itself was the most discriminant condition with 84.7% accuracy (p=0.005). From the oculomotor and vestibular tests, it was found that OKN symptoms were most accurate at 90.3% (p=0.004), followed by the convergence measures at 88.9% (p=0.002), while none of the other outcome measures were retained as significant in a forward conditional regression model. When combining the VR-balance outcomes with the OKN symptoms and the convergence test in a single regression model, accuracy reached 95.8%. Using this model to calculate a receiver operating characteristic curve (Fig. 1) revealed it to have a highly significant area under the curve (AUC=0.985, p<0.001).

4. Discussion

The combination of visuomotor tests that are necessary for spatial and self-motion perception with postural tasks which rely on the integration of visual and vestibular input contributed to the regression model that had the most accurate outcomes for discriminating mTBI health status. The assessment with the portable VR-based balance device alone was able to discriminate between health status groups, with the concussed group showing greater COP sway area and variability than the healthy group. The specific VR condition that was most sensitive to differences involved dynamic visual motion, as has been previously shown with large field-of-view VR in mTBI [24, 45, 46], as well as in other clinical populations with visual vestibular processing deficits [30, 32]. The symptom reports collected after performing the oculomotor and vestibular tests (i.e. rapid alternating horizontal eye saccades, optokinetic stimulation, and the gaze stabilization test) were all sensitive to health status; however, the signs did not show observable abnormalities (i.e. the observable eye movements). Moreover, the BESS, King-Devick, and Dynamic Visual Acuity tests did not detect any significant between-group differences. These findings, discussed below, suggest visual-vestibular processing deficits are present in acute and subacute individuals following mild traumatic brain injury.

Vestibular processing

There are a number of clinical assessments of VOR that are commonly used and three of them were employed in this study (head thrust, DVAT, GST). Despite prior

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evidence that VOR abnormalities are prevalent following mild head trauma [27, 40], the assessment of objective signs that were observed in the current sample of healthy and concussed participants were not found to be sensitive to health status. Two possible reasons for this (which are also applicable to the oculomotor tests discussed later), are that the protocol for subjectively identifying abnormal saccades or loss of target fixation during the tests used in the current study was not sensitive enough to detect deficits or that our raters did not have the requisite level of expertise to reliably detect them. Despite this, the subjectively experienced symptoms reported by the participants after the GST were found to be sensitive to brain injury, with individuals in the concussion group reporting more dizziness, headache, and nausea.

In this study, the insensitivity of the direct tests of peripheral vestibular function such as the DVAT and head thrust and the indirect measures of vestibular function, such as the balance conditions that heavily rely on vestibular input, suggests that the consequences of mTBI are not a purely vestibular system deficit [1]. Specifically, the BESS test conditions performed on foam with eyes-closed provides unreliable somatosensory feedback and no visual feedback, therefore postural control is dependent on vestibular processing. Similarly, the EC-Foam condition on the VR-balance device also relies heavily on vestibular contributions to balance. The vestibular system acts via the descending vestibulospinal and reticulospinal tracts to make postural corrections and maintain upright stability. However, neither the EC-Foam nor BESS foam conditions showed significant between-group differences for health status. It should be noted that the BESS has been shown to return to normal within five days post-injury [22, 37], while the majority of our concussion group was more than two weeks post-injury. Despite this, the evidence suggests that the symptoms being experienced in our concussion group cannot be fully described by vestibular deficits alone.

Visual and oculomotor processing

The oculomotor assessments of *signs* were largely insensitive to health status (i.e. smooth pursuit, KD, HES, OKS) with the exception of near-point convergence. The lack of sensitivity to these assessments may be due to lack of rater expertise, as suggested above, but the extended time-since-injury of the our cohort may have allowed for compensation or recovery to occur. There was, however, evidence that NPC is negatively affected by mild TBI even with the subacute individuals within our cohort, which supports previous findings [10, 47]. The sensitivity of NPC may speak to its ease of use; participants can reliably report when a visual target becomes blurry or doubles and the experimenters could reliably use the tool. Given the discriminant accuracy of NPC found in this study, various mesencephalic circuits are implicated. The ‘near-response’ neurons driving the near-reflex triad (i.e. convergence, accommodation, and pupil constriction) involve the oculomotor and parasympathetic Edinger-Westphal nuclei [36]. These oculomotor control centers and the afferent and efferent white matter tracts linked to these centers, such as the tectospinal or cortico-tectal tracts, may be highly susceptible to the biomechanical stress and strain forces following head impact due to their location in the midbrain [46, 48]. The view that diffuse axonal injury has widespread cortical and subcortical effects following mTBI is generally accepted [6]. Given the presence of oculomotor control deficits it appears brainstem involvement is very likely, while the

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presence of visual motion processing deficits, discussed below, support the idea that the injury is not isolated to the brainstem.

Although the *signs* observed in the oculomotor tests were not sensitive to health status, the reported *symptoms* following some of the oculomotor tests were (i.e. HES and OKS). This symptom sensitivity supports previous reports of symptom elicitation after observing excessive optic flow [29]. Individuals who have recently experienced a concussion or those suffering from unremitting post-concussive symptoms (PCS) often report sensitivity to light and visual motion such as when watching television or playing video games. The oculomotor response during HES and OKS requires the suppression or activation of the optokinetic reflex, respectively. The neural centers and circuitry associated with OKN include many midbrain structures, including the oculomotor and accessory optic nuclei and the nearby optic tract nuclei [9]. These centers have connectivity to the vestibulocerebellum and the visual (parietal-occipital) association cortices. Thus, although the signs were not detected, visual processing associated with the OKN is impaired in a manner that reliably elicits symptoms in those with concussion. This evidence points to a possible combination of cortical and subcortical regions involved in both visual and vestibular processing.

Visual-vestibular processing

Processing of visual motion is integral to self-motion perception and an individual's ability to discern self versus environment motion involves multisensory comparison between vestibular, somatosensory, and visual inputs [52, 55]. The interplay between the neural regions involved in visual and vestibular processing has been shown in behavioral and imaging studies. Regions such as the parieto-occipital and parietal insular vestibular cortex are thought to be reciprocally innervated [7, 51] and together with bidirectional, decussating connectivity to the vestibular nuclei play an important role in postural control, self-orientation, self-motion perception [17, 33]. The oculomotor and vestibular test findings here suggest that the descending visual-vestibular centers at the brainstem level could be affected by damage, however cortical level damage cannot be ruled out when the multisensory deficits seen in the postural tests are considered.

Postural conditions tested with the VR-device provide compelling evidence that post-concussive symptoms involve visual-vestibular integration difficulties. The balance conditions most sensitive to health status were the two dynamic visual roll conditions (DYN-Foam and DYN-Firm). These conditions were designed to be destabilizing by creating a visual-vestibular conflict between subjective visual and gravitational verticals [16, 53]. This destabilizing visual-roll effect is even greater for individuals who have experienced a head impact [46], even when sub-concussive [24]. Other evidence that visual-vestibular processing is disrupted following mTBI comes from a case study involving a patient suffering from severe visual and physical motion intolerance and static balance difficulties a month after the incident [43]. The patient was treated with optokinetic stimulation/habituation, visual/physical perturbations, and postural stability exercises in a large field virtual environment, which resulted in almost complete symptom resolution after six treatments [43]. The current and previous evidence indicates that difficulties in visual-vestibular integration may persist well after the typically suggested resolution period of 7-10 days.

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Conclusions

Our findings suggest that visual-vestibular processing deficits are present in acute and subacute individuals following mild traumatic brain injury. The combination of specific postural tasks designed to assess well-calibrated integration of visual and vestibular inputs together with visuomotor tests that assess spatial and self-motion perception were found to be the most sensitive tests for discriminating health status following mTBI. The comprehensive evaluation of the signs and symptoms allows us to infer which neural processes may be damaged by the injury. It should be noted that assessments largely based on patient reports of symptom provocation rely on the accuracy and integrity of subjective report. Therefore, ensuring subjective measures are supplemented by objective measures such as the VR-based postural assessment described here, ensures higher fidelity in concussion assessment. Finally, this study has not identified nor excluded the etiological role that cognitive, psychogenic, emotional, cellular, and other neurophysiological processes may play in concussion symptomology [3, 6, 50] and these must be considered in any comprehensive multifactorial clinical evaluation of concussion. However, our findings may serve to focus attention in on using sensitive tools for assessing symptoms, especially chronic unremitting symptoms, which can help clinical decision-making and accurate assessment of the recovery process.

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Table 1. Means and standard deviations of concussion assessment scores

Variables	Concussed n = 14 M ± SE	Healthy n = 58 M ± SE	*p*
VR-based Posture			
EO-Firm	0.89 ± 0.08	2.71 ± 1.68	0.15
EC-Firm	1.58 ± 0.16	6.72 ± 4.39	0.13
DYN-Firm	4.76 ± 0.55	25.2 ± 14.3	0.09
EO-Foam	3.46 ± 0.24	10.3 ± 5.71	0.12
EC-Foam	14.9 ± 1.02	26.9 ± 8.78	0.10
DYN-Foam	51.5 ± 4.57	107.3 ± 23.2	0.016*
BESS			
Total	13.4 ± 0.59	11.7 ± 1.26	0.21
Vestibular and Oculomotor Assessments			
NPC	3.42 ± 0.26	6.28 ± 1.04	0.018*
HES Symptoms	0.07 ± 0.04	1.75 ± 0.78	0.050*
OKS Symptoms	0.02 ± 0.02	1.71 ± 0.72	0.035*
GST Symptoms	0.26 ± 0.09	1.64 ± 0.56	0.029*
DVA line difference	1.45 ± 0.19	1.93 ± 0.41	0.27
KD Score	81.0 ± 1.75	89.4 ± 8.59	0.13

Note. M (mean), SE (standard error of the mean), n (number). BESS (balance error scoring system), NPC (near point convergence), HES (horizontal eye saccades), OKS (optokinetic stimulation), GST (gaze stabilization test), DVA (dynamic visual acuity), KD (King-Devick), SP (smooth pursuit), *Significance set at $p \leq 0.05$.

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Table 2. Correlation of Concussion Assessments with Health Status

Variables	*r*	*p*
VR-based Posture		
EO-Firm	0.26	0.030*
EC-Firm	0.28	0.019*
DYN-Firm	0.33	0.005*
EO-Foam	0.28	0.016*
EC-Foam	0.29	0.013*
DYN-Foam	0.42	<0.001*
BESS		
Total BESS Test	-0.15	0.21
Vestibular and Oculomotor Exam		
NPC	0.42	<0.001*
HES Symptoms	0.46	<0.001*
OKS Symptoms	0.50	<0.001*
GST Symptoms	0.45	<0.001*
DVA Line Difference	0.13	0.27
KD Score	0.18	0.13

Note. BESS (balance error scoring system), DVA (dynamic visual acuity), GST (gaze stabilization test), KD (King-Devick), HES (horizontal eye saccades), NPC (near point convergence), OKS (optokinetic stimulation), *r* (Pearson product-moment correlation coefficient), *Significance set at $p \leq 0.05$.

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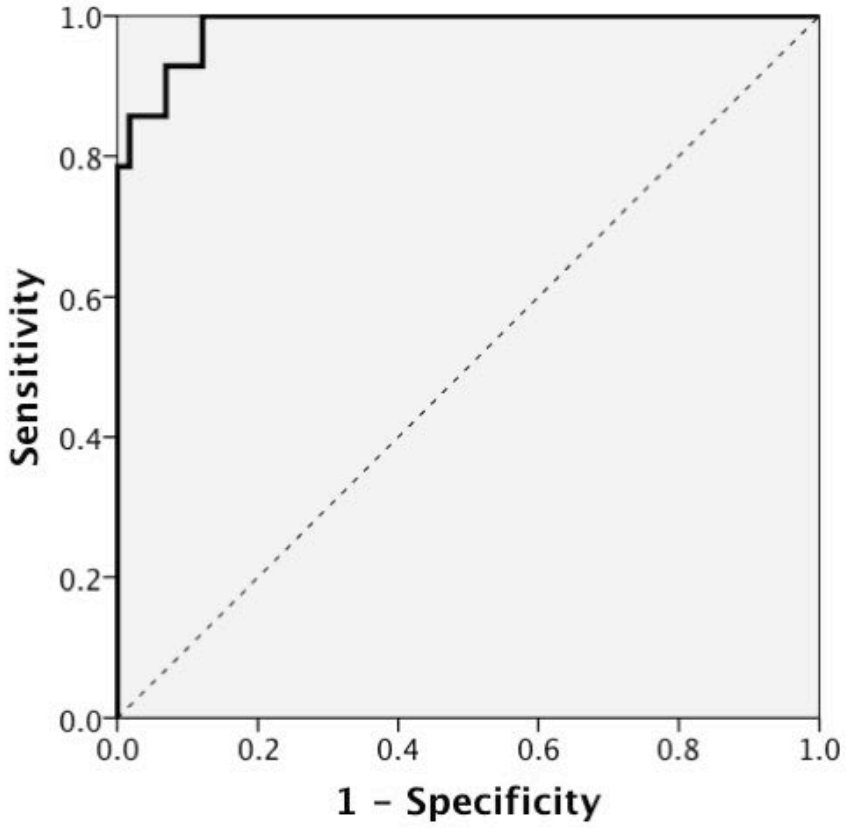

Figure 1. ROC curves generated using a logistic regression model. The model includes the VETS COP sway area (thick black), OKN symptoms, and the NPC distance. The AUC (0.985) is highly significant with an excellent sensitivity and specificity well above chance (dotted diagonal line).

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Appendix 7

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Sensitivity of the Balance Error Scoring System and the Sensory Organization Test in the Combat Environment

F. Jay Haran,[1] Jill C. Slaboda,[2] Laurie A. King,[3] W. Geoff Wright,[4] Daniel Houlihan,[5] and Jacob N. Norris[6]

Abstract

This study evaluated the utility of the Balance Error Scoring System (BESS) and the Sensory Organization Test (SOT) as tools for the screening and monitoring of Service members (SMs) with mild traumatic brain injury (mTBI) in a deployed setting during the acute and subacute phases of recovery. Patient records (N = 699) were reviewed for a cohort of SMs who sustained a blast-related mTBI while deployed to Afghanistan and were treated at the Concussion Restoration Care Center (CRCC) at Camp Leatherneck. On initial intake into the CRCC, participants completed two assessments of postural control, the BESS, and SOT. SMs with mTBI performed significantly worse on the BESS and SOT when compared with comparative samples. When the SOT data were further examined using sensory ratios, the results indicated that postural instability was primarily a result of vestibular and visual integration dysfunction ($r > 0.62$). The main finding of this study was that the sensitivity of the SOT composite score (50–58%) during the acute phase was higher than previous sensitivities found in the sports medicine literature for impact-related trauma.

Key words: BESS; military; mTBI; SOT

Introduction

The U. S. Department of Defense (DoD) defines traumatic brain injury (TBI) as a "traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force."[1] The incidence of TBI in Service members (SMs) has been reported to be as high as 20% with a large majority of these injuries being classified as a mild TBI (mTBI).[2] In combat situations, an undiagnosed or unresolved mTBI can have serious implications for the safety of the SM and their units, because common symptoms of an mTBI include visual alterations, confusion, headaches, dizziness, and vestibular disorders.[3–5] After an mTBI event, a SM may have difficulty concentrating when receiving orders, balance problems when walking on uneven terrains, slowed reaction times, or difficulty making mission critical decisions.[6]

Current DoD policy guidelines in operational environments for return to duty (RTD) decisions after an mTBI are largely based on clinical guidance provided by the sports medicine community for return-to-play decisions.[7–9] These guidelines require mandatory neurological and functional evaluations with military clinicians on a patient's self-reported symptoms (e.g., Neurobehavioral Symptom Inventory), neurocognitive (e.g., Automated Neuropsychological Assessment Metrics), and balance tests (e.g., Romberg test).[10–12] As such, the expected course of recovery for the majority of persons with mTBI typically involves a resolution of clinical symptomology within a week, neurocognitive impairment within 7–10 days, and postural stability (i.e., balance) impairment within 3–5 days.[13–17]

The presentation of mTBI symptoms has been well documented in the sports medicine literature, and some studies have documented similar presentation in military populations for symptom resolution and cognition[18,19]; however, there are only three published articles in the literature pertaining to the presentation and resolution of postural stability impairment in military personnel in a deployed setting.[3,18,19]

One report on mTBI-related postural instability in a military population focused predominantly on an mTBI cohort of SMs with blast exposure who were medically evacuated from the theater and

[1]Navy Experimental Diving Unit, Panama City Beach, Florida.
[2]The Geneva Foundation, Tacoma, Washington.
[3]Department of Neurology, Oregon Health & Science University, Portland, Oregon.
[4]Department of Physical Therapy, Temple University, Philadelphia, Pennsylvania.
[5]Department of Occupational Therapy, Tufts University, Medford, Massachusett.
[6]Neurotrauma Department, Naval Medical Research Center,Silver Spring, Maryland.

evaluated in a tertiary care balance center in the United States.[3] Patients in this study were grouped according to the time of presentation for initial evaluation. For the patients within this cohort who exhibited postural instability, there were significant differences found between patients seen 4 to 30 days after blast exposure and those evaluated more than 30 days after blast exposure as indicated by the Sensory Organization Test (SOT; NeuroCom International Clackamas, OR). Postural stability was found to be worse in those seen more than 30 days after blast exposure, suggesting that postural instability in subjects worsens over time; however, the groups were distinct, and patients were not tracked over time.

The study also had a small group of patients seen within 72 h of blast exposure, but they were not evaluated using the SOT. These patients were evaluated in the combat zone while chronic patients were those evacuated from the combat zone; acute and chronic patients may have had qualitatively different injuries. In addition, the population tested included SMs with acute blast exposure, and the results may not be applicable to persons with blunt- or impact-related mTBI.

The aforementioned postural assessment measure, the SOT, is one of the most commonly used assessments and has been shown to be a viable measure for assessing balance after a concussion.[13] The SOT uses a force plate system with a moveable visual surround to systematically disrupt the sensory selection process by altering the orientation information available to the somatosensory and/or visual inputs.[20] Responses to balance perturbations and the person's ability to maintain quiet stance are recorded through the force plates, and customized software provides a composite equilibrium score.

The practicality and accessibility of the SOT has been questioned because it requires the NeuroCom Smart Balance System (NeuroCom, subsidiary of Natus Medical Inc., Pleasanton, CA), which has a large footprint and would not be easily accessible in a forward-deployed operational setting.[20] The SOT has been reported to have a low to moderate diagnostic accuracy (sensitivity 34–38% and specificity 88–95% using a 90% confidence interval [CI]) to classify the presence of an mTBI within the acute (i.e., <5 days post-injury) phase of recovery.[21,22] In addition, it has been recommended that the SOT be administered twice on the same day to achieve moderate to good reliability estimates (0.51 to 0.64) across all of the test conditions.[23]

The remaining two reports focused on the same mTBI cohort of SMs with blast exposure who were seen either at the Concussion Restoration Care Center (CRCC) at Camp Leatherneck, (AFG) or Kandahar Air Field (KAF), Bagram Air Force Base.[18,19] Balance was evaluated with the Balance Error Scoring System (BESS) twice, once 0–7 days (acute phase of recovery) after blast exposure in AFG and again 6–12 months (chronic phase of recovery) on their return to the United States. The results indicated that balance was not significantly impaired at either assessment when the SMs with mTBI were compared with an age-matched control group of enlisted men.

It should be pointed out that when a nonage-matched control group was used for comparison, there were significance differences found for the acute assessment. In addition, the researchers make a point to indicate that both the mTBI group and the control groups performed worse than the normative performance of collegiate athletes[14] extracted from the sports-related mTBI literature.

The BESS is a clinically oriented balance assessment that does not need sophisticated technology, yet it is still able to provide a quantifiable method of assessing balance.[24] The BESS is a brief, easy to administer, and transportable assessment that is widely accepted and emerging as the gold standard for assessing mTBI-related postural instability in a nonlaboratory setting.[20,25] The BESS requires a foam pad and a stopwatch. Individuals perform a series of stances with and without visual input while being scored for errors by trained individuals.

The BESS has been clinically validated and reported to have a low-to-moderate diagnostic accuracy (sensitivity 10–34% and specificity 91–93% using a 90% CI) to classify the presence of an mTBI within the acute phase of recovery.[14,26–28] Despite its ease of use, the BESS still has limitations because it is prone to learning effects and subjectivity, and may only have moderate interrater reliability (0.57 to 0.85).[25,29,30] In addition, it has been recommended that the BESS be administered at least three times within the same day to achieve a good test-test reliability estimate.[31]

To date, there have been no studies that have documented the clinical utility of the SOT and BESS in the combat environment. Namely, no study has evaluated the sensitivity of either assessment to blast-related mTBI in a combat setting during the acute and subacute phases of recovery. The purpose of this effort was twofold: (1) determine if there are significant differences in postural stability between a comparative sample and a cohort of SMs who sustained an mTBI while deployed to Afghanistan and were treated at the CRCC, and (2) describe the sensitivity of the BESS and SOT using reliable change methodology. With respect to the first aim, we hypothesize that BESS and SOT scores from the deployed mTBI population will be significantly different from comparative scores derived from a healthy cohort found in the literature.

Methods

The study was a retrospective cross-sectional analysis of patient record information collected and maintained in the locally obtained clinic database. This was part of a process improvement effort to document injuries, evaluations, and treatments and to chart the recuperative course of patients. The study was approved by the US Naval Medical Research Center Institutional Review Board, which granted a waiver of informed consent. All data were collected in compliance with the regulations of the Institutional Review Board. All data was de-identified before analysis.

Record screening

Record flow is illustrated in Figure 1. CRCC records from August 2010 to November 2012 were screened from the CRCC patient database using the following inclusion criteria: diagnosis of a concussion by a CRCC provider based on DoD definition of mTBI/concussion[9]; blast-related injury mechanism; no previous concussions treated at the CRCC; no reported musculoskeletal injuries that would hinder performance on any of the assessment measures; known date of injury; record for either an initial SOT and BESS, which was performed at intake into the CRCC. Additional inclusion criteria for the BESS record sample only was being male to match all-male no-concussed active duty comparative sample.[18]

The initial set of patient records ($n = 699$; age = 25.08 ± 4.46 years) were primarily enlisted members (96%) from the Marines (76%) and Army (20%) with a minimal concussion history (0.94 ± 1.44). After applying the inclusion criteria, 203 records for the SOT and 131 for the BESS remained for analysis. It should be noted that not all SMs who had data for the BESS had data for the SOT because the SOT was not integrated in the CRCC clinical assessment protocol at the same time as the BESS was introduced at the CRCC. Available demographics for the BESS record sample indicated that the sample was 100% male, the mean age was 24.36 ± 5.64 years (range 19–51), and the mean time from injury was 6.43 ± 11.96 days (range 0–104). There was no statistical difference in age between the SOT and BESS samples ($p = 0.26$).

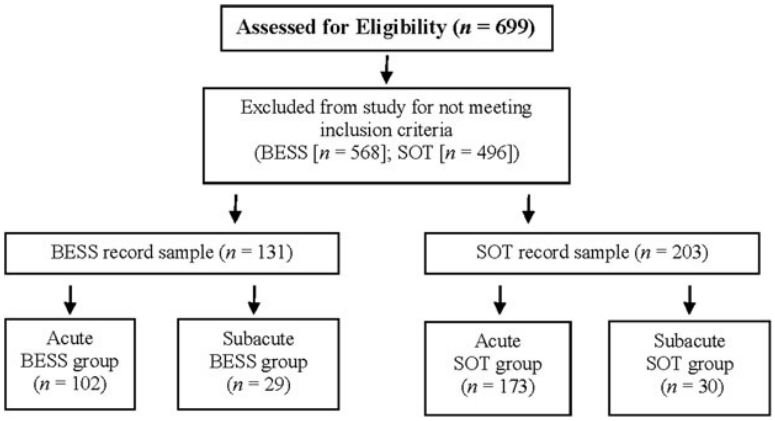

FIG. 1. Flowchart for inclusion and exclusion criteria. BESS, Balance Error Scoring System; SOT, Sensory Organization Test.

Group assignment

Records were then assigned to one of two independent groups for each measure (i.e., two independent SOT groups and two independent BESS groups) based on the time from injury to the time when initial intake assessment was performed at the CRCC. The acute groups consisted of SMs who were initially assessed during the acute phase (i.e., ≤7 days post-injury).[32] The subacute groups consisted of SMs who were initially assessed during the subacute phase (i.e., 8–89 days post-injury).[32]

Group assignment for the SOT record sample resulted in 173 SMs being assigned to the acute SOT group (mean age 25.63 ± 2.64; mean time from injury 2.64 ± 1.54 days) and 30 to the subacute SOT group (mean age 24.57 ± 5.14; mean time from injury 15.33 ± 10.40 days). Group assignment for the BESS record sample resulted in 102 SMs being assigned to the acute BESS group (mean age 24.30 ± 5.83; mean time from injury 2.83 ± 1.78 days) and 29 to the sub-acute BESS group (mean age 25.00 ± 10.78; mean time from injury 15.50 ± 13.50 days).

Instrumentation

The BESS uses a combination of three different stances: narrow double leg stance (feet together), single leg stance (standing on the nondominant leg), and a tandem stance (feet placed heel to toe). Each stance was performed on a firm surface and compliant foam for a total of 6 conditions. For each condition, patients were instructed to place their hands on their hips, close their eyes, and remain as motionless as possible for 20 sec. Patients were instructed to return to the testing position as quickly as possible if they lost their balance or fell out of their respective test stance.

Performance was scored by adding 1 point for each error committed. Common errors include but are not limited to: lifting hands off the hips; opening eyes; stepping, stumbling, or falling; movement of the hip into more than 30 degrees; lifting the forefoot or heel; and remaining out of the testing position for more than 5 sec. Trials were considered incomplete if a patient could not maintain the stance position for longer than 5 sec and was given the maximum score of 10 points. The total number of errors for each test condition were recorded and summed to produce the total BESS score.

The SOT consists of three different visual conditions (eyes open, eyes closed, sway referenced) and two different support surface conditions (stationary, sway referenced). Each visual condition was paired with each support surface for a total of six conditions. The six conditions were as follows: eyes open and stationary support surface (condition 1), eyes closed with stationary support surface (condition 2), sway-referenced visual surround with stationary support surface (condition 3), eyes open with sway-referenced support surface (condition 4), eyes closed with sway-referenced support surface (condition 5), sway-referenced visual surround and sway-referenced support surface (condition 6). Each condition was repeated three times for a total of 18 trials.

Embedded software provides a composite score (CS), a weighted average representing the magnitude of body sway in the anterior-posterior direction and indicates the overall level of performance during all the trials, with higher scores being indicative of better balance performance. The software also calculates ratio scores for each sensory input that represent relative differences between the equilibrium scores of certain trials to indicate specific information regarding balance for each sensory input.

These ratios can be used to identify difficulties in using a particular sensory system for balance. The somatosensory ratio (SOT_SOM) was calculated by comparing condition 2 with condition 1. This ratio indicates the subject's ability to use input from the somatosensory system to maintain balance. The visual ratio (SOT_VIS) was calculated by comparing condition 4 with condition 1. This ratio indicates the subject's ability to use input from the visual system to maintain balance. The vestibular ratio (SOT_VES) was calculated by comparing condition 5 with condition 1. This ratio indicates the subject's ability to use input from the vestibular system to maintain balance.

Data analyses

All analyses were performed with Matlab 2013b (Mathworks, Natick, MA) and SPSS Version 22 (IBM, Armonk, NY). Descriptive statistics were calculated for each continuous variable (i.e., BESS and each SOT-derived outcome score).

Because there were no baseline data available or normative data for healthy, nonconcussed active duty SMs for either the BESS or SOT, comparative samples were identified and extracted from the literature. The comparative sample used in the analyses for the BESS was from data collected from an all-male, age-matched (range 19–48) healthy, nonconcussed active duty population (N = 64), who were receiving care at the CRCC or KAF for minor nonblast-related musculoskeletal injuries.[18] The comparative sample used in the analyses for SOT-derived outcome scores was collected from data for 63 young nonconcussed healthy adult collegiate athletes.[21] Unfortunately, these data were a subset of the study's overall sample (N = 75), and no demographics for the subset were reported.

The normal distribution of the raw data for each continuous variable was assessed using the Shapiro-Wilk test. Because all continuous variables were found to be not normally distributed, simple

Table 1. Descriptive Statistics for the Comparative Data and Concussion Restoration Care Center Service Members

	Norms			*CRCC*					
Outcome score	*N*	*M*	*SD*	*N*	*M*	*SD*	*MDS*	*z*	*ES*
SOT CS[19]	63	82.39	5.7	203	70.11	13.97	−8.39*	−9.40	0.66
SOT SOM[19]	63	96.39	2.96	203	94.16	7.71	0.61	0.98	0.07
SOT VIS[19]	63	93.41	5.13	203	74.12	18.57	−15.41*	−12.21	0.86
SOT VES[19]	63	76.93	9.17	203	57.30	20.21	−15.93*	−8.84	0.62
BESS[32]	64	15.42	8.89	133	24.03	11.36	6.58*	5.59	0.48

CRCC, Concussion Restoration Care Center; N, number of participants; M = mean; SD, standard deviation; MDS, median normative difference score; *z*, z-statistic; ES, effect size, *r*. *, significant differences at $p \leq 0.05$.

difference scores (i.e., CRCC assessment score–comparative sample mean) were used to determine changes in performance. Four one-sample sign tests were conducted for the SOT difference scores to determine whether the mean of the difference scores was equal or less than zero. One-sample sign tests were conducted for the BESS difference scores to determine whether the mean of the difference scores was equal or greater than zero. Effect size was calculated as *r*. Mann-Whitney *U* tests were used to compare groups. Alpha was set at $p = 0.05$ using a Bonferroni-Holm correction. The number of tests within each assessment was used to determine the Bonferroni-Holm correction.

Reliable change parameters were used to provide a cut-score from whether a change from a comparative sample mean was real, reliable, and clinically meaningful, or if it fell within the normal variance in performance and/or measurement error.[33–35] Reliable change cut-scores for each SOT-derived outcome score were extracted from the literature.[4] These cut-scores were calculated using the Jacobson and Truax method with an adjustment for practice effects using a 90% CI and an 80% CI. The extracted cut-scores were then applied to difference scores to assess the number of SMs who had reliable decreases in performance relative to the comparative sample, represented by decrease in the SOT-outcomes scores, at each CI.

Because there were no reliable change cut-scores for the BESS found in the literature, cut-scores were calculated using the Jacobson and Truax method with no adjustment for practice effects.[35,36–38] Standard deviation (SD) and intraclass correlation ($ICC_{(2,1)}$) values were used to estimate the standard error of measurement (SEM), which was then used to calculate the standard error of the difference (S_{diff}) and create a CI for each difference score.[39,40] SEM was calculated from using SD and $ICC_{(2,1)}$ from comparative data extracted from the literature.[18,41] The estimated S_{diff} values were multiplied by a value from the *z*-distribution to calculate a CI for the difference scores. The formulae that were used are as follows:

$$SEM = SD\sqrt{1 - ICC_{(2,1)}}$$

$$Estimated\ S_{diff} = \sqrt{2SEM^2}$$

$$80\ CI = (Estimated\ S_{diff} * 1.28)$$

$$90\ CI = (Estimated\ S_{diff} * 1.64)$$

The leading tail of each CI was used as a cut-score. The cut-scores were then applied to post-injury difference to assess the number of SMs who had a reliable decrease in performance, represented by increased BESS scores, at each CI.

Results

Table 1 contains descriptive statistics for the comparative data, overall record sample, acute group, and subacute group. The data were run with parametric and nonparametric statistics with agreement between the two analyses; however, only the nonparametric results are reported because of normality violations. The result for the one-sample sign-test for the BESS data revealed statistically significant differences ($p < 0.0001$, one-sample sign test), with the median of the difference scores being greater than zero. There were no differences in performance between the acute and subacute groups ($p = 0.49$, Mann-Whitney *U* test). The results for the one-sample sign-test for the SOT data revealed statistically significant differences for SOT_CS ($p < 0.001$, one-sample sign test), SOT_VIS ($p < 0.001$, one-sample sign test), and SOT_VES ($p < 0.001$, one-sample sign test), with the median of the difference scores being lower than zero.

In contrast there was no significant difference for SOT_SOM ($p = 0.441$, one-sample sign test). There were also no significant differences in performance between the acute and subacute groups for any of the SOT-derived outcome scores ($p > 0.11$, Mann-Whitney *U* tests).

Table 2 includes the number and percentages of SMs broken down by group who had scores below the cut-score (i.e., lower scores) on the SOT and above the cut-score BESS (i.e., higher

Table 2. Percentage of Sample Identified with Lower Scores Within Each Group

			Acute group		*Subacute group*	
CI	*Outcome score*	*Actual cut-score*	N	%	N	%
90% CI						
	SOT CS	74	87	50%	14	47%
	SOT SOM	88	20	12%	3	10%
	SOT VIS	83	111	64%	15	50%
	SOT VES	55	60	35%	7	23%
	BESS	11	36	35%	9	31%
80% CI						
	SOT CS	75	100	58%	14	47%
	SOT SOM	89	28	16%	4	13%
	SOT VIS	85	121	70%	17	57%
	SOT VES	58	82	47%	8	27%
	BESS	9	40	39%	9	31%

CI, confidence interval; N, number of Service member records; %, percentage of Service member records; SOT, Sensory Organization Test; CS, Composite Score; SOM, Somatosensory Ratio; VIS, Visual Ratio; VES, Vestibular Ratio; BESS, Balance Error Scoring System.

scores) when compared against the comparative sample. The percentages of SMs who were identified as having low scores for the BESS ranged from 31% for the subacute group at the 90% CI to 39% for the acute group at the 80% CIs. The percentages of SMs who were identified as having low scores for the SOT ranged from 10% for SOT_SOM for the subacute group at the 90% to 70% for SOT_VIS for the acute group at the 80% CI.

Discussion

This study evaluated balance data (i.e., BESS and SOT) that were collected in a theater of operations from a cohort of SMs with a diagnosis of mTBI, yet not evacuated out of theater. SMs with mTBI performed significantly worse on the BESS and SOT when compared with their respective comparative means. These findings indicate that both assessments were able to illicit postural instability in SMs recovering from mTBI during the acute phase of recovery and that the assessments can be used as part of an in-theater return-to-duty assessment.

Perhaps the most important finding in this retrospective analysis was that the sensitivity of SOT_CS (50–58%) during the acute phase (~3 days post-injury event) was higher than sensitivities that have been reported for the SOT (SOT_CS = 38%, 1 day post-injury event)[21] in the sports-related (blunt) mTBI literature. In addition, postural instability did not resolve, but rather continued—albeit, at a slightly lesser rate into the subacute phase (SOT_CS = 47%). This finding is also not in agreement with the sports-related mTBI literature, where it is commonly accepted that postural stability typically returns to normal within 3–5 days post-injury.[14,26–28]

The recovery timeline observed in the current study may be the result of the different injury mechanisms and resulting neuropathophysiology from blast and blunt trauma. Blunt trauma typically results in coup and countercoup injuries with localized diffuse axonal damage, whereas blast trauma typically results in widespread periventricular injury.[42–45] There is also evidence from the clinical setting, which indicates that blast and blunt traumas result in differing patterns of dizziness and instability with blast-exposed persons reporting more severe symptoms.[3,5,46–51]

Postural stability is thought to be maintained through corrective actions governed by a central processing of afferent input from the somatosensory, vestibular, and visual systems. Postural instability after mTBI has been suggested to be a result of a sensory interaction problem that prevents accurate use and/or exchange of information at either the central or peripheral level or both.[52,53] The results of the SOT indicate that SMs had the greatest difficulty balancing under the conditions involving an unstable support surface and either normal ($r = 0.86$) or absent vision ($r = 0.62$).

This result is not unexpected, because blast exposure is associated with dizziness, vertigo, oscillopsia, vertical hyperphoria, accommodation issues, smooth-pursuit problems, and saccadic eye movement dysfunction.[3,48,50,54–58] It is difficult to truly parse out, however, which system is more adversely affected without a full neurological examination because the vestibular and visual systems are tightly linked via the vestibulo-ocular reflex and optokinetic reflex, especially during a complex multisensory task such as maintaining normal balance.

Several aspects of the current study warrant special considerations. The comparative samples were used out of convenience because there is a gap in the literature in regard to military-specific normative data, stratified by age and/or gender, for both the BESS and the SOT. Even though the comparative sample used in the BESS analyses was age and gender matched, the ICC value extracted from the literature was calculated from a sample that was not (healthy young adults (N = 30; 50% male; mean age, 24.4 ± 3.9 years).[41] In addition, we did not adjust the cut-scores for practice effects, which may have artificially increased the number of SMs above the cut-score.

The comparative sample used in the SOT analyses was not an active duty population, but rather a healthy collegiate athletic population.[21] Although the military cohort we tested is perhaps comparable in fitness level to collegiate athletes, moderators related to the stressful environment of forward deployment, such as dehydration and fatigue, may have contributed to the differences found.[59,60] In addition, the SOT comparative sample was not age matched, and age has been shown to be highly correlated with postural instability in concussed persons.[61]

There was no attempt made to control for possible confounding variable such as anthropometrics (i.e., body mass index, and height)[62] and comorbid conditions (i.e., post-traumatic stress disorder or depression or current musculoskeletal pain/ injury)[63] that may have altered the results. The applicability of our findings to the overall military may be limited because our data were primarily from Marines injured in AFG from 2010 to 2012, and the nature of these operations may not be representative of future conflicts. Finally, this study was unable to address the specificity of the SOT and BESS because it did not include a cohort of noninjured controls.

These limitations aside, this study had notable strengths; it furthers our understanding using under-utilized approaches. First, it is the largest single dataset of concussed patients from a combat zone to be assessed in the acute and subacute phases after the mTBI-causing event. Second, this study leverages a well-documented methodology, reliable change, to address the highly relevant need to understand the measurement properties of commonly used mTBI assessments. Finally, these data suggest that greater attention may need to be focused on characterizing the pathophysiological differences between blunt trauma and blast trauma.

Conclusion

This study reports on the sensitivity component of clinical utility of the BESS and SOT to identify mTBI within the combat environment. The main finding of this study is that both assessments were able to detect postural instability in SMs recovering from mTBI during the acute and subacute phases of recovery. Thus, either assessment could be included in any in-theater return-to-duty decision as part of a multidimensional assessment that includes: a clinical assessment, survey of symptomology resolution, and neurocognitive testing. In addition, the results of the SOT outcome measures may illuminate slight differences between blunt trauma and blast mTBI, which may provide further insight into the pathophysiology that is causing the symptoms associated with TBI.

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Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:
Jacob N. Norris, PhD
Neurotrauma Department
Naval Medical Research Center
Silver Spring, MD 20910

E-mail: jacob.n.norris.mil@mail.mil

Appendix 8

NAVAL POSTGRADUATE SCHOOL

MONTEREY, CALIFORNIA

THESIS

BASELINE ESTABLISHMENT USING VIRTUAL ENVIRONMENT TRAUMATIC BRAIN INJURY SCREEN (VETS)

by

Casey G. DeMunck

June 2015

Thesis Advisor:	Lee Sciarini
Second Reader:	Joseph Sullivan

This thesis was performed at the MOVES Institute

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The Virtual Environment Traumatic Brain Injury Screen (VETS) prototype was designed to enable the assessment of mild traumatic brain injury (mTBI). This research aims to establish baseline data for balance as an indicator for mTBI and determine reliability of the VETS device. Objectives of this research were to examine the within-session and between-day performance of four balance-based indictors of mTBI with a healthy military population. Fifteen healthy individuals participated in two sessions, separated by a week, where they were tested under six conditions for three trials each. Balance data were recorded by the VETS system using a Wii Balance Board with participants in a quiet stance. In-session performance was examined using a paired-samples t-test. A repeated-measures ANOVA was used to individually examine differences between trials across both sessions. A final repeated-measures ANOVA was used to explore all trials across both sessions. Results revealed that the participant performance remained constant or improved across trials and sessions suggesting that a practice effect may have occurred in some conditions. These results suggest that the VETS device reliably measures balance as an indicator of mTBI. Further, these results establish a baseline data set, which may be useful in comparing concussed individuals.

14. SUBJECT TERMS

Concussion, mild traumatic brain injury (mTBI), traumatic brain injury (TBI), balance, Sensory Organization Test, Balance Error Scoring System, center of pressure, Virtual Reality, diagnosis, commercial off-the-shelf, Wii Balance Board, Virtual Environment

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BASELINE ESTABLISHMENT USING VIRTUAL ENVIRONMENT TRAUMATIC BRAIN INJURY SCREEN (VETS)

Casey G. DeMunck
Major, United States Marine Corps
B.S., United States Naval Academy, 2003

Submitted in partial fulfillment of the
requirements for the degree of

MASTER OF SCIENCE IN MODELING, VIRTUAL ENVIRONMENTS, AND SIMULATION

from the

NAVAL POSTGRADUATE SCHOOL
June 2015

Author: Casey G. DeMunck

Approved by: Lee Sciarini
Thesis Advisor

Joseph Sullivan
Second Reader

Christian Darken
Chair, MOVES Academic Committee

Peter J. Denning
Chair, Department of Computer Science

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ABSTRACT

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List of Acronyms and Abbreviations

ACH	Advanced Combat Helmet
ANOVA	analysis of variance
AP	anterior posterior
BESS	Balance Error Scoring System
COP	center of pressure
COTS	commercial off-the-shelf
CT	computed tomography
CTSIB	Clinical Test for Sensory Integration of Balance
DOD	Department of Defense
FDA	Food and Drug Administration
GCS	Glasgow Coma Scale
GUI	graphic user interface
HMMWV	Highly Mobile Multipurpose Wheeled Vehicle
HSI	Human Systems Integration
ICU	Intensive Care Unit
IED	improvised explosive device
IRB	institutional review board
JIEDDO	Joint Improvised Explosive Device Defeat Organization
LOC	loss of consciousness
LVS	Logistics Vehicle System

LVSR	Logistics Vehicle System Replacement
LWH	Lightweight Helmet
MACE	Military Acute Concussion Evaluation
MICH	Modular Integrated Communications Helmet
ML	medial lateral
MRAP	Mine Resistant Ambush Protected
MRI	magnetic resonance imaging
mTBI	mild traumatic brain injury
MTV	Medium Tactical Vehicle
MTVR	Medium Tactical Vehicle Replacement
NFL	National Football League
NIJ	National Institute of Justice
NPS	Naval Postgraduate School
OEF	Operation Enduring Freedom
OIF	Operation Iraq Freedom
PASGT	Personnel Armor System for Ground Troops
PTSD	Post Traumatic Stress Disorder
RMS	root mean square
SAC	Standardized Assessment of Concussion
SOCOM	Special Operations Command
SOT	sensory organization test

SPSS	Statistical Package for the Social Sciences
SSQ	Simulator Sickness Questionnaire
TBI	traumatic brain injury
TTP	tactics, techniques, and procedures
U.S.	United States
USAF	United States Air Force
USA	United States Army
USMC	United States Marine Corps
USN	United States Navy
VE	virtual environment
VETS	Virtual Environment Traumatic Brain Injury Screen
WBB	Wii Balance Board

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CHAPTER 1:
Introduction

1.1 Overview

The condition traumatic brain injury (TBI) is a temporary or permanent neurological dysfunction caused by an external force on the body. TBI can also result from the body being shaken violently or being in an accelerated state and stops suddenly. In the military domain, TBI typically results from an individual being exposed to the effects of explosions. Effects can be direct, as when the shock wave of an explosion passes through the skull, or indirect, as when an individual is thrown and his or her head impacts another object. The injury can be "open," as a visible injury to the head, or "closed," as with internal injury of the brain with no visible external injury. TBI is classified into three levels of severity: mild traumatic brain injury (mTBI), moderate, and severe. This thesis focuses on closed mTBI.

Compared to previous conflicts, Iraq and Afghanistan have resulted in increased explosive-related injuries to the head and neck. Injuries to the head and neck have increased to 30 percent of injuries sustained by military personnel, up from 21 percent during World War II [1]. The injury mechanism during current conflicts is predominately caused by explosions, 81 percent of injuries, as opposed to gunshot related injuries, 19 percent of injuries. Of diagnosed TBI in military personnel, mTBI comprises 77 percent of the cases [2], [3].

During the final stages of conflict in Operation Enduring Freedom (OEF)/Operation Iraq Freedom (OIF), there was a mandatory minimum 24-hour rest period if military personnel are exposed to the effects of an explosion, regardless of whether the individual is showing signs of mTBI [4]. To work, this system relies heavily on self-reporting, evaluation by deployed medical personnel, and leaders educated in the effects of mTBI. In the distributed and remote nature of deployments, such as to Afghanistan, medical personnel may not be present to prescribe bed rest for 24–96 hours. Due to manpower constraints, it may not be tactically feasible to place all personnel who felt the effects of an explosion on bed rest for that time frame. For example, if an explosion occurs next to a mine-resistant vehicle carrying eleven people, under the current standard all eleven should be placed on bed rest

at the earliest possible time, even though only one may be showing symptoms of mTBI.

Symptoms of mTBI can manifest themselves in three different categories: alterations of the somatic system, cognitive ability, and psychological effects. Impacts to the somatic system can result in headaches, dizziness, and degradation of the senses [5]. Cognitive effects express themselves as memory loss, inability to pay attention, or difficulty with common tasks such as speech. Psychological repercussions include changes to personality, depression, anxiety and, in extreme cases, suicidal tendencies. Additionally, mTBI is also linked with Post Traumatic Stress Disorder (PTSD) due to the often traumatic nature of mTBI producing events and an evaluation for PTSD should be considered if an individual is diagnosed with a TBI [5].

Immediate treatment of mTBI centers on reducing the risk of another concussion in the days after the first event. If an individual receives ample rest and treatment of symptoms shortly after a mTBI producing event, his or her chances of long-term neurological dysfunction are greatly reduced [5]. If, however, an individual is exposed to additional mTBI-producing events after the first incident, his or her chances of long-term adverse effects are increased [6].

1.2 Background

Screening methods for mTBI range from biomarkers in the bloodstream to cranial ultra sounds [7]. These procedures require medical facilities and trained personnel to administer them. One screening method is to test balance. Mild TBI has an adverse effect on the vestibular system and thus compromises the individual's ability to balance. Typically, this is not visible in a person affected by mTBI due to the body's ability to compensate for a degraded vestibular system by using visual cues and the somatic system to determine the individual's orientation relative to the ground. If a person affected by mTBI stands on an unstable surface, such as foam, which isolates the somatic system, and is told to close his or her eyes, he or she will be unable to balance or find it extremely difficult to do so, as the injured vestibular system is not functioning properly [8]. This is a prime indicator of mTBI but does not serve as a diagnosis [9].

The VETS device [10] isolates the vestibular system as a way to screen for potential mTBI. By using a virtual environment, visual cues to the user can be controlled to remove reliance

on ocular input. A Wii Balance Board (WBB) is used as an input device to measure how well the user is balancing. Foam can be added on top of the board to reduce the somatic system's ability to compensate for a degraded vestibular system. This device has the potential to be used as a low-cost screening tool in a deployed environment in order to target mTBI treatment for those who need it most.

1.3 Objectives

This thesis studies human subjects using the Virtual Environment Traumatic Brain Injury Screen (VETS) device [10] to collect baseline data on a healthy military demographic. The goal of this study will be to establish a norm for which individuals with possible mTBI symptoms can be screened. To this date, a healthy military population baseline has not been established using the VETS device. Additionally, the feasibility of the VETS device as a low-cost screening tool utilized in a deployed environment will be evaluated.

If a healthy military population baseline for balance can be established using the VETS device, then the device can potentially be used as a low-cost portable screening tool for concussion injuries. This can provide the Department of Defense (DOD) with an effective tool for detecting potential mTBI far forward in a deployed environment, which will greatly enhance an affected individual's chances of a speedy recovery and potentially reduce incidence of subsequent concussions.

1.4 Scope and Limitations

If we think of a TBI producing event, an acute injury, as being at the middle of a spectrum, there is a wide spectrum of research and effort before and after that event. Considerable focus is placed on prevention and detection of an injury event in the form of a material or doctrinal solutions. Additionally, there is a tremendous effort in expanding treatment techniques after TBI has been detected. This study will focus on a potential method of detecting TBI directly following an acute injury. The primary domain of this study is military usage, although there are potential benefits to the athletic community. Participants for this study represented an age demographic (M=33, SD=5) slightly higher than the DOD mean. Figure 1.1 shows an age group breakdown of the active duty portion of the DOD during 2013. Participants of this study represent approximately 15% of the DOD [11].

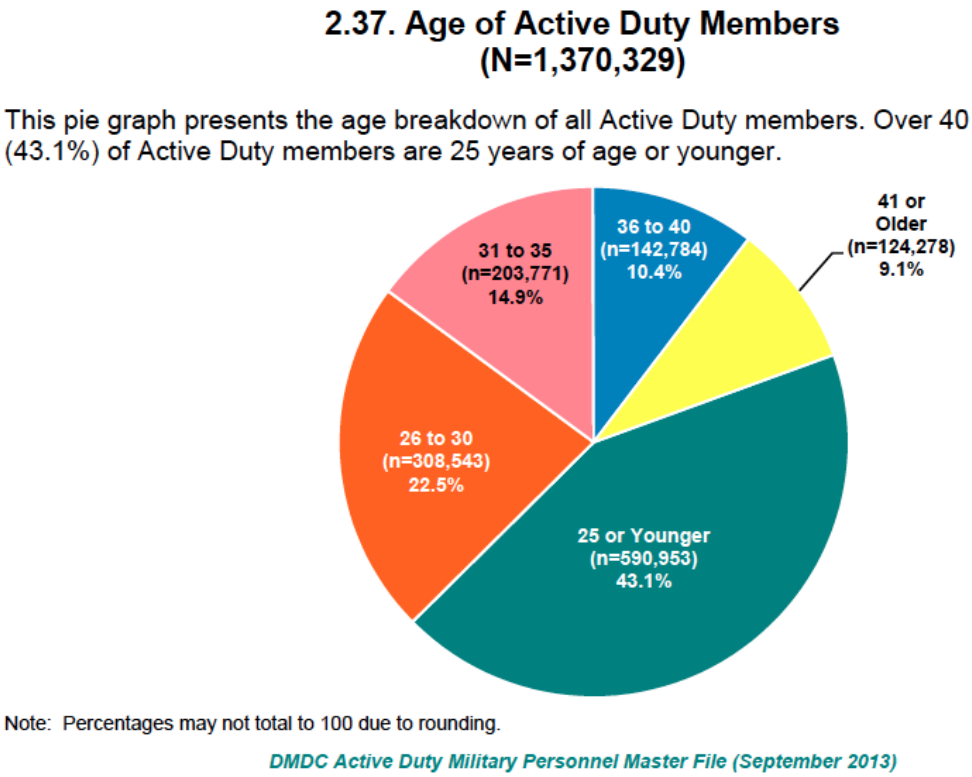

Figure 1.1: Age breakdown of all DOD active duty members for 2013. This year was the latest data available, from [11].

1.5 Thesis Organization

The rest of the thesis is organized as follows: Chapter 2 provides a literature review beginning with an overview of the prevalence of TBI and associated issues facing the DOD concerning TBI. The utilization of virtual environment (VE) as a diagnostic tool for neurological disorders and a summary of findings. Chapter 3 outlines the methodology utilized for this study. The overall design of the study, participant recruiting, implements used, and data collection are explained. Chapter 4 provides an analysis of collected data and discussion of results. Chapter 5 contains conclusions and recommendations resulting from the study and the author's evaluations.

CHAPTER 2:
Literature Review

Individual safety encompasses a wide range of subjects in the military domain. Training mishaps, enemy threats, and industrial accidents are a few of the hazards facing service members. Guidance for the acquisition of military equipment dictates that Human Systems Integration (HSI) specifically be utilized to consider occupational hazards and force protection issues [12]. In the context of head injuries, there is a significant body of research with the sole purpose of protecting and caring for a service member. If one thinks about an event that causes mTBI as being on a time line at zero, with actions leading up to that event occurring to the left and actions after the event to the right, there are distinct areas of research along that entire spectrum, see Figure 2.1. This chapter will provide a brief overview of those areas and describe the focus of this thesis.

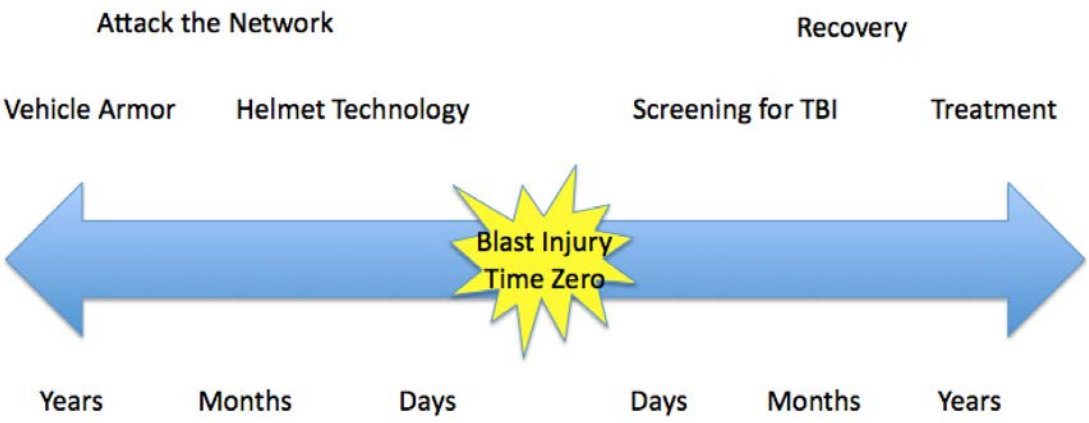

Figure 2.1: Time line of events surrounding a head injury event. Actions to the left of the blast are aimed at protection and prevention. Actions to the right of the blast are aimed at detection of a TBI and treatment in the long term.

2.1 Traumatic Brain Injury

One challenge facing mTBI research is simply determining an exact definition of the injury [13]. TBI is categorized in three different levels of severity; low, mild, and severe. The level

of severity does not directly correlate to potential for long-term ill effects. An individual can have a mild injury that has lasting negative effects on his or her quality of life [6]. It is further described by mechanism of injury: open or closed. Open-head trauma contains visible wounds and closed-head trauma shows no visible wounds.

Traumatic brain injury occurs when there is an associated head trauma or a sudden acceleration/deceleration force felt by the head. Unique to the military, are blast waves produced by explosions passing through the brain, resulting in trauma. During this trauma, the neurons that form connections in the brain literally shear apart and cease to function properly. The level to which shearing occurs and location of shearing depends largely on the severity of the injury itself. The result is improper neurological function as the brain attempts to reestablish broken connections between neurons [6].

For this thesis, mTBI describes a closed brain injury that results in altered cognitive, neurological, and/or physiological function.

2.2 Protection

Given that the mechanism of injury is typically trauma or a sudden jerk force, the immediate solution that comes to mind is to protect the individual's body from the force. Innovation in protecting the individual has accelerated over the last decade and continues to focus on HSI during acquisition [12]. These improvement are represented by Figure 2.1 in the years and months leading up to a potential injury event. Protection is broken into two categories here, one for personal body armor and one for vehicular armor.

2.2.1 Helmet Technology

When the first United States troops set foot in Afghanistan in early winter of 2001 and in Iraq in March of 2003, they were wearing Personnel Armor System for Ground Troops (PASGT) helmets designed and fielded in the early 1980s. While the helmet had not changed much in twenty years, it did offer National Institute of Justice (NIJ) Level IIIA protection. Level IIIA provides protection against handgun rounds up to a 240gr .44 Magnum bullet traveling at 1340 ft/s and fragmentation [14]. Figure 2.2 gives a sense of scale for body armor, there are two more levels above Level IIIA that encompass rifle rounds. The PASGT had no padding inside, a chin strap attached at two points, and a leather sweat band

attached with webbing inside the helmet. Though this setup provided protection against ballistic threats, it provided little in the way of impact/shock protection for the individual wearing it [15].

Armor Level	Protection
Type I (.22 LR; .380 ACP)	This armor would protect against 2.6 g (40 gr) .22 Long Rifle Lead Round Nose (LR LRN) bullets at a velocity of 329 m/s (1080 ft/s ± 30 ft/s) and 6.2 g (95 gr) .380 ACP Full Metal Jacketed Round Nose (FMJ RN) bullets at a velocity of 322 m/s (1055 ft/s ± 30 ft/s). It is no longer part of the standard.
Type IIA (9 mm; .40 S&W; .45 ACP)	New armor protects against 8 g (124 gr) 9x19mm Parabellum Full Metal Jacketed Round Nose (FMJ RN) bullets at a velocity of 373 m/s ± 9.1 m/s (1225 ft/s ± 30 ft/s); 11.7 g (180 gr) .40 S&W Full Metal Jacketed (FMJ) bullets at a velocity of 352 m/s ± 9.1 m/s (1155 ft/s ± 30 ft/s) and 14.9 g (230 gr) .45 ACP Full Metal Jacketed (FMJ) bullets at a velocity of 275 m/s ± 9.1 m/s (900 ft/s ± 30 ft/s). Conditioned armor protects against 8 g (124 gr) 9 mm FMJ RN bullets at a velocity of 355 m/s ± 9.1 m/s (1165 ft/s ± 30 ft/s); 11.7 g (180 gr) .40 S&W FMJ bullets at a velocity of 325 m/s ± 9.1 m/s (1065 ft/s ± 30 ft/s) and 14.9 g (230 gr) .45 ACP Full Metal Jacketed (FMJ) bullets at a velocity of 259 m/s ± 9.1 m/s (850 ft/s ± 30 ft/s). It also provides protection against the threats mentioned in [Type I].
Type II (9 mm; .357 Magnum)	New armor protects against 8 g (124 gr) 9 mm FMJ RN bullets at a velocity of 398 m/s ± 9.1 m/s (1305 ft/s ± 30 ft/s) and 10.2 g (158 gr) .357 Magnum Jacketed Soft Point bullets at a velocity of 436 m/s ± 9.1 m/s (1430 ft/s ± 30 ft/s). Conditioned armor protects against 8 g (124 gr) 9 mm FMJ RN bullets at a velocity of 379 m/s ±9.1 m/s (1245 ft/s ± 30 ft/s) and 10.2 g (158 gr) .357 Magnum Jacketed Soft Point bullets at a velocity of 408 m/s ±9.1 m/s (1340 ft/s ± 30 ft/s). It also provides protection against the threats mentioned in [Types I and IIA].
Type IIIA (.357 SIG; .44 Magnum)	New armor protects against 8.1 g (125 gr) .357 SIG FMJ Flat Nose (FN) bullets at a velocity of 448 m/s ± 9.1 m/s (1470 ft/s ± 30 ft/s) and 15.6 g (240 gr) .44 Magnum Semi Jacketed Hollow Point (SJHP) bullets at a velocity of 436 m/s (1430 ft/s ± 30 ft/s). Conditioned armor protects against 8.1 g (125 gr) .357 SIG FMJ Flat Nose (FN) bullets at a velocity of 430 m/s ± 9.1 m/s (1410 ft/s ± 30 ft/s) and 15.6 g (240 gr) .44 Magnum Semi Jacketed Hollow Point (SJHP) bullets at a velocity of 408 m/s ± 9.1 m/s (1340 ft/s ± 30 ft/s). It also provides protection against most handgun threats, as well as the threats mentioned in [Types I, IIA, and II].
Type III (Rifles)	Conditioned armor protects against 9.6 g (148 gr) 7.62x51mm NATO M80 ball bullets at a velocity of 847 m/s ± 9.1 m/s (2780 ft/s ± 30 ft/s). It also provides protection against the threats mentioned in [Types I, IIA, II, and IIIA].
Type IV (Armor Piercing Rifle)	Conditioned armor protects against 10.8 g (166 gr) .30-06 Springfield M2 armor-piercing (AP) bullets at a velocity of 878 m/s ± 9.1 m/s (2880 ft/s ± 30 ft/s). It also provides at least single hit protection against the threats mentioned in [Types I, IIA, II, IIIA, and III].

Figure 2.2: National Institute of Justice ballistic standards for body armor, after [14].

In the early 2000s, United States (U.S.) Special Operations Command (SOCOM) adopted the Modular Integrated Communications Helmet (MICH) as their standard helmet. The MICH offered slightly less coverage to accommodate communications headsets, lighter weight, and increased impact protection for the individual. The suspension/retention system in the MICH used a four-point strap system for increased stability on the individual's head. The leather sweat band and strap harness inside the PASGT was replaced by a foam padding system designed to absorb and dissipate impact [15].

The success of the MICH prompted the United States Army (USA) and United States Marine Corps (USMC) to use it as the basis for a replacement to the PASGT. In 2003, the Army adopted the Advanced Combat Helmet (ACH), which used shock-resistant padding and more robust retention systems to reduce impact related injuries. The Marine Corps chose the Lightweight Helmet (LWH) as a replacement and began fielding it in 2003. Al-

though an improvement over the PASGT, the early versions of the LWH did not have shock absorbing padding inside. The padding system of the LWH was not changed until several years later [16].

Improvements in ballistic protection and impact absorption have mitigated two main threats from blast injuries. Objects in motion impacting an individual's head and the body being thrown against something are indirect results of an explosion. Atmospheric over pressure is the primary result of explosions and produces a blast wave that travels through the body [15]. This blast wave predominately has adverse effects on the ears, lungs, and bowels, where liquids and gasses mix, but it can also produce a shearing effect among the brain's neurons. Despite these advancements in protective helmets, there remains no way to prevent explosive over pressure from traveling through the body [2].

2.2.2 Vehicle Armor

During the initial invasion of Iraq and Afghanistan between 2001 and 2003, support vehicles lacked the robust armor. The Army's and Marine's primary wheeled vehicles for troop and cargo transport, the Highly Mobile Multipurpose Wheeled Vehicle (HMMWV), Medium Tactical Vehicle (MTV), and Logistics Vehicle System (LVS) had little need for armor until this most recent conflict [1]. Logistics support and large troop transportation took place in the rear area which was considered safe until the early stages of OEF and OIF. These vehicles valued speed and cargo/troop carrying capacity over protection. Most provided little more than thin metal or canvas between the occupants and outside.

The most protected troops on the battlefield were those in armored units who utilized tanks and fighting vehicles on the front lines. With the advent of improvised explosive device (IED) to attack comparatively more vulnerable support troops, the incidence of blast-related injuries climbed. This increase resulted in blast injuries accounting for the majority of hazards on the modern battlefield [1]. As a result, armor kits were designed to retrofit existing vehicles and new vehicles were purchase with armor and survivability as a primary goal, such as the Mine Resistant Ambush Protected (MRAP) family of vehicles. While increased vehicle armor has saved many service member's lives, the risk of having a brain injury when involved in an IED blast inside one of the vehicles still remains [2].

2.3 Prevention

While protection is aimed at placing a barrier in between the individual and a hazard, prevention is aimed at avoiding the hazard all together. In the case of avoiding IEDs, being able to identify then reduce the threat and removing an enemy's capability to use IEDs as a weapon are the two main avenues of approaching the problem.

2.3.1 Removing the Hazard

As a result of the increased usage of and casualties from IEDs, the Army established an IED Task Force in 2003 with the main focus of reducing this threat [17]. From this task force, Joint Improvised Explosive Device Defeat Organization (JIEDDO) was born in 2006. DOD Directive 2000.19E formally established JIEDDO as a jointly manned activity and specified its mission, function, and authority [18]. During OEF and OIF, JIEDDO formed several subordinate task forces that were geographically specific to analyze threats unique to Afghanistan or Iraq.

JIEDDO employs a three pronged approach to removing or reducing explosive hazards on the battlefield. A robust intelligence capability allows them to track and identify bomb makers, financiers, suppliers, and emplacers. The goal here is to "attack the network" by removing one or multiple components necessary for the enemy to use IEDs against US forces [17]. Leveraging technology and a rapid acquisition ability, JIEDDO aims to "defeat the device" used against deployed troops [17]. Developing techniques and technology to detect, neutralize, and mitigate explosive hazards support this portion of their mission. The last approach used is a robust training effort to educate service members on the most up to date threats, how to plan for, avoid, and react to explosive hazards on the battlefield. Training programs range from detailed explanation of construction and employment of IEDs to increased observational skill sets such as the Marine Corps' Combat Hunter program [19]. This thrust is also the lead for developing doctrine and tactics, techniques, and procedures (TTP) for combating this threat [17].

2.4 The Injury

The aforementioned methods greatly increased the safety of service members in deployed environments, but IEDs remained a significant threat. Once a blast injury affects service members, the focus shifts to detection of an injury and treatment. In obvious cases of

individuals with a severe open TBI, they are removed from the battlefield at the soonest tactical convenience through casualty evacuation procedures. Those with no visible signs of injury will likely remain on the battlefield, even if they are experiencing the effects of mTBI.

In order to provide effective treatment as early as possible, it is necessary to determine if an individual has symptoms of a TBI. If an individual has a closed injury and does not experience a significant loss of consciousness (LOC), as in a momentary LOC, or no LOC at all, they will likely not know to self report a possible TBI. This becomes especially challenging in the chaos of a high stress combat scenario where an individual may not realize or remember there was a LOC or degraded cognitive performance. Since early detection and treatment are key to full recovery from a mTBI, simple and effective screening aides are important to target treatment to those who need it and return to duty those who so no signs of an injury [5], [13], [20]. An individual is particularly at risk of long lasting adverse effects if they receive a second TBI in the following days/weeks from their first [3], [5]. This may be a result of sustained combat operations where it is not tactically feasible to screen individuals for potential TBI immediately. When it is feasible to screen for TBI with tools that have limited impact on combat operations (ie. where service members do not need to be transported to a specialized facility with highly skilled medical personnel), the opportunity should be taken [20].

2.5 Assessing TBI

There are numerous methods used to determine if someone is suffering from mTBI. Detection methods range from objective measures such as blood sample analysis and magnetic resonance imaging (MRI) brain scans to subjective measures which are often in the form of verbally administered tests. This injury presents a challenge for diagnosis due to its often subtle and highly variable effects.

2.5.1 Objective Measures

Objective means for determining if a mTBI is present aim to accurately quantify some nature of the injury by a test. This often involves some specialized equipment to measure results and for the test itself. An objective test also has the potential of being more reliable as the effect of inter-rater reliability and bias is reduced [21], [22].

Objective detection methods that require specialized highly sensitive equipment, skilled technicians to operate, laboratories to test results, or that require lengthy lead times are not feasible in deployed austere environments specific to the military domain. Though a service member might be able to receive an MRI in a military hospital in Germany within 24 hours of the time they were injured in a mature theater such as Iraq, there is no guarantee that such services will be widely available to deployed personnel. The military requirements for an accurate detection method are something that will withstand the rigors of frequent transport and in less than surgery room levels of cleanliness, is easy to use, and presents real time results [7].

2.5.2 Neuroimaging

A common tool used to assist clinicians in determining a possible TBI is neuroimaging. The two most commonly used methods are computed tomography (CT) and MRI scans, with CT scans providing lower fidelity to the later [22]. Neither is used as a stand alone tool for assessing potential TBI, but used to assist the clinician with a determination. The decision to use one of these scans is not automatic when assessing a patient. If there are warnings and indicators of a TBI (such as a self reported LOC less than 30 minutes or visible trauma), a neuroimaging scan will likely be ordered. Patients with more subtle symptoms may not receive a scan [23].

The CT scan is most commonly used due to the speed of evaluation and lower cost. Despite these advantages, a CT scan can only detect anomalies in the physical structure of the brain and has a potential health risk associated with ionizing radiation used for the scan. The main advantage of CT scans are the detection of intracranial lesions, which serve as a prime indicator of the presence of a TBI although a TBI may exist with no intracranial lesions [22], [23].

A MRI is a more expensive and time consuming alternative to the CT scan and does not pose a risk from ionizing radiation. The advantage of an MRI is its ability to assess physical structure and function of the brain. This ability provides more insight into the nature of an injury on an individual and can greatly assist a clinician in making a determination. However, there is a possibility that an MRI will show normal function even if the individual has a TBI [22], [23].

Despite their advantages, these detection methods remain on the higher end cost, and require dedicated infrastructure and personnel to operate. These qualities preclude their use on a mass scale in an austere environment.

2.5.3 Other Objective Methods

There are other objective measures for potentially detecting the presence of a mTBI that are less mature but worthy of note none-the-less. Placing sensors in an individual's helmet to detect impact force and using blood tests near the point of injury.

Sensor systems placed in helmets gained interest with the DOD shortly after the National Football League (NFL) began using them in player's helmets [7]. The basic premise for the multiple sensor systems on the market is the same, place a data recorder in a helmet with an accelerometer to determine if an individual has been exposed to sufficient impact, acceleration, or deceleration to warrant further investigation. While this technique has shown positive results in the relatively controlled environment of the football field, it has mixed reviews in the military domain [7]. The primary detractors from using sensor systems are the number of false positives, sensor orientation, reading data from a large number of helmets, and cost. Military helmets take a large amount of abuse, while being worn and when not being worn. Some of this abuse is sufficient enough to trigger a positive reading, such as a helmet falling off the hood of a vehicle when not being worn. Most sensors on the market also require a specific orientation to function correctly, which is not feasible in the military domain. Once data is collected it must be transferred to, and read by, someone who can interpret it. These factors make current sensor technology cost prohibitive for large forces [7].

Using blood chemistry as an indicator of a mTBI, when no visible signs of behavioral change exist, is a promising realm of objective measures [7]. Testing methodology involves taking a blood sample from potentially affected individuals in the field and analyzing the sample on location. Potential candidates for biomarkers include: S100B, glial fibrillary acidic protein, and neuron-specific enolase [7]. The two main challenges associated with this method are the development of an effective field portable test and Food and Drug Administration (FDA) approval of these markers as an indicator of mTBI.

2.5.4 Balance

Sustaining a mTBI has an acute effect on an individual's ability to balance in the subsequent days following an injury. As the body attempts to repair the broken connections of neurons in the brain resulting from an injury, it increases its glucose metabolism for a period of approximately six hours following injury [8]. After this period, glucose metabolism slows to an abnormal rate for up to five days. The result of this imbalance is an adverse effect on the individual's ability to maintain balance [8], [24].

Objective measures of balance can be conducted using computerized dynamic posturography, where a computer assesses balance through the use of a force plate and visual inputs [25]. Medical grade devices, such as the NeuroCom EquiTest, use a sensory organization test (SOT) to measure balance. The SOT assesses the three components of balance through six conditions of varying visual and somatic input. The SOT uses sway, the anterior posterior (AP) and medial lateral (ML) movement of an individual, to score balance on a 100 point scale with the high end being perfect balance and a score of zero showing no ability to balance. This test has shown degraded balance ability in individual's affected by a TBI [25], [26].

Similar to the SOT, the Clinical Test for Sensory Integration of Balance (CTSIB) assesses postural stability through four conditions of varying degrees of visual and somatic input [27]. It uses a sway index as the standard deviation from the individual's average center of mass. Similarly, computerized dynamic posturography devices use this technique to assess balance. Specifically, the Biodex Balance System and BioSway utilize this technique [27].

The use of an individual's center of pressure (COP) is a common method used to measure balance [28]. One can think of COP as an individual's center of mass projected down to the ground, representing the point over which the center of mass is located. Measuring the movement of COP falls into two main categories: how far it moves, sway, and how fast it moves, velocity. The use of COP sway and velocity as an indicator of postural control has been proven as a reliable method with velocity providing the best indicator [28], [29], [30].

These devices, while cheaper than a MRI or CT scan, cost in the tens of thousands of dollars range. While popular with the professional sports and physical therapy industry, they do not offer the portability or ease of use needed in the austere environment of deployed

troops. There are conflicting opinions concerning the usefulness of quantitative balance measures. In particular, some researchers suggest that subjective screening tests are just as effective in diagnosing TBI [31] while others consider the use of devices capable of accurately measuring balance as a more effective method for assessing TBI [31], [32].

2.5.5 Subjective Measures

Subjective measures for evaluating individual's with potential TBI are typically administered by a clinician familiar with the screening method. They are observational in nature with written results being tallied for a final score that serves as an indicator. They have the advantage of being able to be administered in most settings and are simple to use. However, reliability between administrators is questionable [7], [31].

Glasgow Coma Scale

The Glasgow Coma Scale (GCS) was developed by Graham Teasdale and Bryan J. Jennett at the University of Glasgow's Institute of Neurological Sciences in 1974 [33]. It was originally designed to assess a patient's level of consciousness in an Intensive Care Unit (ICU) setting though it is now widely used by clinicians and first responders to assess head injuries. The assessment tests eye, verbal, and motor responses and assigns a score according to the level of response. Scores range from 0 to 15 (the original scale used a high score of 14 and has since been modified to 15) with 0 being completely unresponsive and 15 indicating potential for a mTBI. These scores are used to indicate the severity of a head injury and provide an indicator if one exists. Figure 2.3 shows the rating system. Much of the literature reviewed uses the GCS as a comparison standard for other methods of determining a TBI [31], [33].

The literature reviewed suggests that there is no single standard for representing a score for a TBI on the GCS. Some literature indicates a mTBI being present with a GCS of >13, while others use a GCS of >12. Severe TBI has a score of <8 in some literature and <9 in others. Moderate TBI exists on the range between theses scores. Figure 2.4 shows one version of level of severity of TBI on the GCS [5], [31].

Even though the GCS has been demonstrated to be a useful, easy-to-use tool capable of evaluating the severity of a TBI [7], it does rely on a clinician's observations and is subject to inter-rater reliability concerns. For example, in 2004, Gill, Reiley, and Green in-

Response	Score
Eye opening	
Opens eyes spontaneously	4
Opens eyes in response to speech	3
Open eyes in response to painful stimulation (eg, endotracheal suctioning)	2
Does not open eyes in response to any stimulation	1
Motor response	
Follows commands	6
Makes localized movement in response to painful stimulation	5
Makes nonpurposeful movement in response to noxious stimulation	4
Flexes upper extremities/extends lower extremities in response to pain	3
Extends all extremities in response to pain	2
Makes no response to noxious stimuli	1
Verbal response	
Is oriented to person, place, and time	5
Converses, may be confused	4
Replies with inappropriate words	3
Makes incomprehensible sounds	2
Makes no response	1

Figure 2.3: Evaluation criteria for the modified Glasgow Coma Scale, after [33].

TBI Classification	Length of Loss of Consciousness	Length of Amnesia	Glasgow Coma Scale Score
Mild TBI (mTBI)	< 20 minutes	< 24 hours	GCS > 13+
Moderate TBI	> 20 minutes, but < 6 hours		GCS 9 - 12
Severe TBI	> 6 hours		GCS < 8

Figure 2.4: Traumatic Brain Injury classification criteria using the modified Glasgow Coma Scale, after [33] .

vestigated the reliability of the GCS in an emergency room setting. The researchers examined 116, independently assessed GCS scores made by emergency physicians. Their results demonstrated that only moderate agreement (32%) exists between raters total GCS scores [21].

Military Acute Concussion Evaluation

Military practitioners developed and adopted an assessment similar to the GCS into the Military Acute Concussion Evaluation (MACE). The MACE is a verbally administered assessment conducted by a trained clinician that includes an examination, details of the nature of the injury, and symptoms experienced by the patient. The two main portions of the MACE include the individual's history of possible mechanisms for head trauma and observations of examination results by the clinician. The second portion utilizes the Standardized Assessment of Concussion (SAC) to measure cognitive performance. The SAC has a scoring range of 0 to 30 with a rating of 24 as the generally accepted threshold

indicator for a possible TBI (higher scores indicate reduced likelihood of a TBI) [34]. It serves as a screening tool to assist medical providers in determining if a TBI is present.

Though the MACE is a valuable tool to assist medical providers in screening individual's with a potential TBI, there are challenges and limitations associated with its use. Despite being an easy to follow guide (see Appendix A), standard training and evaluation for the use of the MACE is lacking with military medical providers [35]. Since no individual baseline score is maintained for an individual evaluated using the MACE, the individual may score at or below the accepted threshold without having a TBI [34], [35]. Additionally, a study conducted by R. L. Coldren et. al [35] suggests the MACE lacks the sensitivity necessary to detect a mTBI past 12 hours from the time of injury.

2.6 Virtual Environments Diagnosis and Treatment

The use of VE for the treatment of varying medical conditions is a domain that has shown promising results, particularly with psychological or neurological disorders [36], [37]. Though the treatment realm has shown the successful use of VE, use in the diagnosis realm has not shown the same advancement [38]. Virtual environments offer unique advantages for use in aiding the diagnosis of psychological and neurological disorders. Their use provides a controlled, tailorable, and safe environment where measurements can be precisely recorded. In cases where the VE is used to replace a test setting, say a planning task to shop for groceries as a test of executive dysfunction, use of a VE was just as good, and better in some regards to the real world test setting [38], [39]. In some cases, testing conditions are not feasible using real world environments, such as a spinning room or using an object to solicit a fear response. The relative ease of being able to create or adjust a testing environment and having the capability to measure dependent variables associated with a particular test make the utilization of a VE viable for obtaining an objective measure for potentially indicating a TBI.

2.7 Summary

The shift in mechanism of injury during recent conflicts and advancements in protective equipment have resulted in an increase in proportion of blast inflicted head trauma casualties. There have been significant efforts to prevent these injuries from happening and in treatment once they occur. A necessary prerequisite for treating brain injuries is utilizing

an effective screening technique to target treatment for those individuals who need it most. Requirements for an accurate detection method in the military domain are a system that will withstand the rigors of frequent transport, performs in austere environments, is easy to use, and presents real time results [12]. Detection methods that require specialized highly sensitive equipment, skilled technicians to operate, laboratories to test results, or that require lengthy lead times are not feasible in deployed austere environments specific to the military domain. Though a service member might be able to receive an MRI in a military hospital in Germany within 24 hours from the time they were injured in a mature theater such as Iraq, there is no guarantee that such services will be widely available to deployed personnel in the future. While simple to use, subjective measures are largely guidelines which are open to the interpretation and observation of the individual administering the test. Having an objective measure, suited for use in an expeditionary environment, to assist medical providers in the diagnosis of a TBI would be beneficial. Of particular interest to the research conducted for this thesis is the use of balance as an indicator of potential head trauma.

The portion of the time line of events surrounding a blast injury, see Figure 2.1, that this thesis focuses on is the period of hours and days directly following an injury producing event. Measuring balance with the aide of a VE using commercial off-the-shelf (COTS) technology is the method chosen in this thesis for ultimately attempting to determine the presence of a mTBI. The use of VETS has potential to be a feasible test in a austere deployed environment.

This thesis aims to determine the reliability of the VETS device as an objective evaluation tool for balance using human subject research. Also, the feasibility of this device for use in the military domain will be investigated. The device measures COP sway and velocity, and root mean square (RMS) AP and ML. The primary focus of analysis with center on COP sway and velocity due to its proven reliability for measuring postural control.

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CHAPTER 3:
Methodology

3.1 Overview

This chapter focuses on the overall setup and execution of human subject testing with the VETS device. Details about the VETS device and procedures participants were asked to perform are explained. The purpose of this chapter is to provide a guide that may be used for repeatability of the experiment.

3.2 Participants

The population of interest is active duty US military personnel. Per Naval Postgraduate School's approved institutional review board (IRB), subjects were recruited from the student body. Appendix B includes a copy of the institutional review board approval for this study. Recruitment occurred through flyers and word of mouth. No special skill sets or experience was necessary for potential subjects. Subjects were excluded from the study if they had sustained a documented head injury within the last month. This condition did not apply to any volunteer and all were able to participate in the study. Appendix C is an example of the recruitment flyer.

3.3 Apparatus

The VETS device includes all electronics, peripherals, foam pad, and accompanying stands needed to conduct testing. An updated software suite to control all components, provide a VE, and collect data is used as well.

3.3.1 VETS

The hardware includes several basic pieces; a large television screen, a computer, a Wii Balance Board, and an Airex foam pad. All components fit onto a metal TV stand with an adjustable height, wheels, and a platform at waist level.

Software

The VETS software suite collects data, using a Wii Balance Board as an input device, at 100 Hz. This collection rate is comparable to medical grade balance research devices such as Natus Medical Incorporated and AMTI Biomechanics force plates [9].

The VETS software suite requires the user to create a Vets/Results directory within the Asus minicomputer's Documents folder prior to install. The purpose of the directory is to provide the software suite a dedicated location to store collected data. Within Results, VETS software creates folders for each run of an experiment.

Once the Results directory has been created and the balance board paired, VETS software will function properly. Double clicking on the desktop VETS shortcut will start the software suite, which automatically detects the presence of the balance board. The graphic user interface (GUI) is a window with four main options at the top. The "Live" option provides a Cartesian Coordinate grid with a blue dot indicating the center of balance detected by the balance board. This section is dynamic and gives a visual indicator of movement by the user as indicated by the blue dot, which shifts according to the user's balance. The "Results" option provides bar graphs indicating differing results according to four measures of effectiveness (MOE). The "Settings" option allows for various runs of the experiment to be selected individually, at random, or in a standard format. Runs of the experiment include; still scene no foam, still scene with foam, eyes closed no foam, eyes closed with foam, dynamic scene no foam, dynamic scene with foam. The "Play" option allows a session name to be input by the user and for the duration of the experiment to be input in seconds.

Once all desired settings are input an experiment can be run. The software suite collects data automatically during each run and saves the data set as an Excel document in the Results directory. Overall, the software is relatively straightforward to operate. There are several acronyms used for the MOE that need to be explained as to what they are measuring and in what units. Data in the Excel file appears to be x and y coordinates for the center of balance from the balance board over time, but again no explanation of what is being measured appears in the Excel file.

Computer

The computer, which will control the visual output to the user and collect balance data from the WBB, is an Asus VM60. This is part of Asus's VivoPC line of non-traditional desktops as it is about the size of a Java textbook and is advertised as being a "mini" computer with the power of a full sized desktop. The computer runs Windows 8 with a 1.8 GHz processor and 4 GB of RAM.

Display

The television, used to provide the visual conditions, is a LG 60-inch 1080P resolution Light Emitting Diode (LED) screen.

Input Devices

The balance board is the standard Wii model produced by Nintendo. The dimension the user has to stand on is approximately 20 inches by 12.4 inches and is 2.1 inches tall. The WBB can accommodate users weighting up to 330 pounds. Peripherals include wireless keyboard and mouse to control the computer along with necessary cables to connect the components.

3.3.2 Questionnaires

Surveys were used to assist in determining possible confounding factors among subjects and to determine if the VETS device might have any adverse affect on subjects. Two surveys were used to accomplish this, a demographic survey and a simulator sickness questionnaire.

Demographics Survey

A demographic survey is administered prior to the VETS battery. The demographic survey includes questions about the subject's age, height, weight, handedness, military service, and if they have been diagnosed with a concussion in their life. Appendix E is an example of the demographic survey.

Simulator Sickness Questionnaire

A standard simulator sickness questionnaire was used to determine if the VETS Virtual Environment had an adverse affect on subject [40]. The questionnaire was administered

prior to the VETS battery. Subjects were asked if any of the conditions listed on the questionnaire had increased or decreased during the experiment. Appendix D is an example of the simulator sickness questionnaire.

3.4 Implementation and Data Collection

3.4.1 VETS

The vets software suite has the capability to measure balance under six different conditions. There are two platform conditions and three visual conditions. The user can either stand on a bare WBB or stand on the WBB with an Airex foam pad on top. Visual conditions include a static scene consisting of a VE scene, a rotating VE scene, and a blank scene in which the user closed their eyes. The leading edge of the WBB was placed 16 inches from the TV to provide for more immersion. Figure 3.1 shows a demonstration of the VETS device. The individual in the picture is not a participant in the study and is only posing for a demonstration photo. Also of note, participants in the study were not wearing their shoes during testing and the WBB was closer to the display platform.

Visual conditions began once the investigator started recording data and ended after 30 seconds. Examples of the visual scenes show the exact scenes a participant would see. Figure 3.2 shows an example of the static scene. Figure 3.3 shows the blank scene in which participants were instructed to close their eyes and maintain balance. At the end of 30 seconds, the participant was told to open their eyes and prepared for the next testing condition. Figure 3.4 shows an instantaneous screen shot of the dynamic scene. This scene was the same picture from the static scene rotated about several axes. The rotational direction, clockwise or counterclockwise, changed between trials.

Subjects attended two testing sessions with the second session occurring a week after the first. A longitudinal study was chosen to determine reliability of the VETS device and to investigate if a change index exists when using the device. Each session consisted of six different testing conditions conducted three times each for a total of 18 trials per session. Each trial lasted for 30 seconds of data collection, between trials subjects were given a rest period. The first three trials in a session were standard (eyes open firm board, eyes closed firm board, and dynamic foam board) with the remaining 15 conditions being randomly presented.

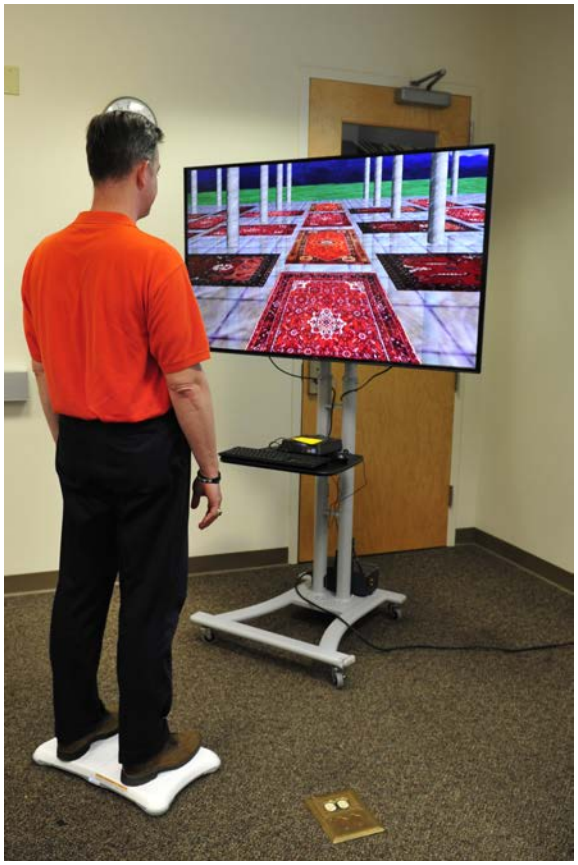

Figure 3.1: Demonstration photo of an individual, not a study participant, using the VETS device. Of note, participants did not wear shoes during testing and the WBB was much closer to the display platform.

The VETS software suite takes input from the WBB and calculates four different measurements to give an indication of balance. For each condition, COP sway area in cm^2, COP velocity in cm/sec, RMS AP in cm, and RMS ML in cm are measured and recorded. The COP can be thought of as a participant's center of gravity projected onto the WBB in two dimensions. Sway area is a measure of the area covered by the COP. RMS AP and ML measure the root mean squared of the forward and back movement and left and right movement respectively. These measurements give an indication of balance ability for the participant [8], [31].

For each participant, the investigator manually inputs testing information into the VETS software suite. Subject identification number, trial length, and condition order are all se-

Figure 3.2: Static visual scene presented to the participant during testing. Participants maintained balance as best as possible for 30 seconds while viewing this scene.

lected from graphic user interface (GUI) such as in Figure 3.5. Once all parameters are set, testing can begin.

3.5 Data Entry and Formatting

It was necessary to consolidate data from the VETS software suite and questionnaires into one master document for ease of analysis. Excel was chosen for the master document for its compatibility with Statistical Package for the Social Sciences (SPSS) and ability to process simple statistics on demographic information.

3.5.1 VETS

The VETS software suite produced 540 Excel files for the 15 participants who took part in this study. Each Excel file contained coordinate data for COP over time and four measurements for each condition. These measurements were copied and input into the master Excel file by subject, session, trial, and condition.

Figure 3.3: Blank visual scene presented to the participant during testing. Participants maintained balance as best as possible for 30 seconds during this scene. Once the screen went to black, the participants were instructed to close their eyes during the test. When the 30-second trial was finished, the investigator informed the participants that they could not open their eyes.

3.5.2 Questionnaires

Demographic Survey

Demographic data collected from surveys were manually input into the master Excel data document. Participants were identified by subject identification number, not by personally identifiable information.

Simulator Sickness Questionnaire

Nothing of significant interest was found after reviewing Simulator Sickness Questionnaire (SSQ) data collected from participants. As such, this information was not captured in the master Excel data document.

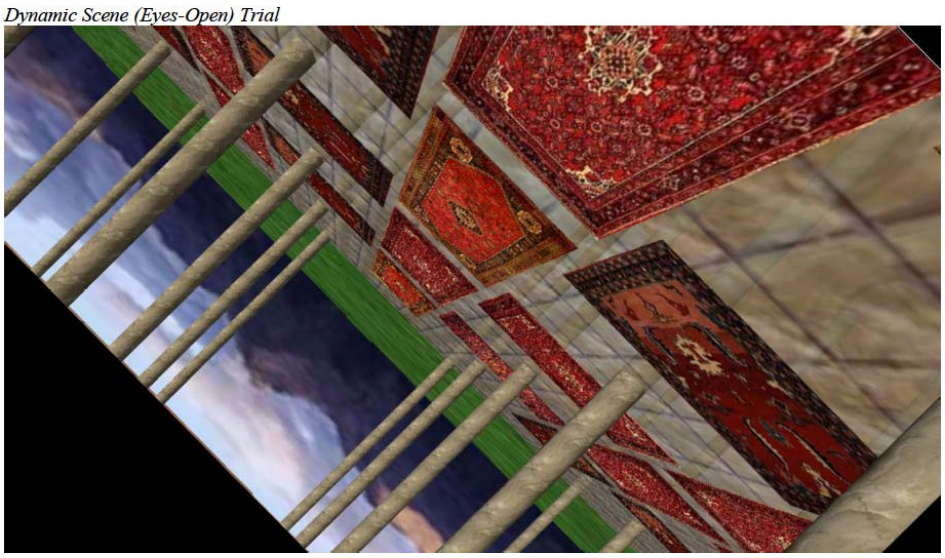

Figure 3.4: Dynamic visual scene presented to the participant during testing. Participants maintained balance as best as possible for 30 seconds while viewing this scene. The dynamic scene rotated about several axes. The direction of rotation, counterclockwise or clockwise, changed between trials.

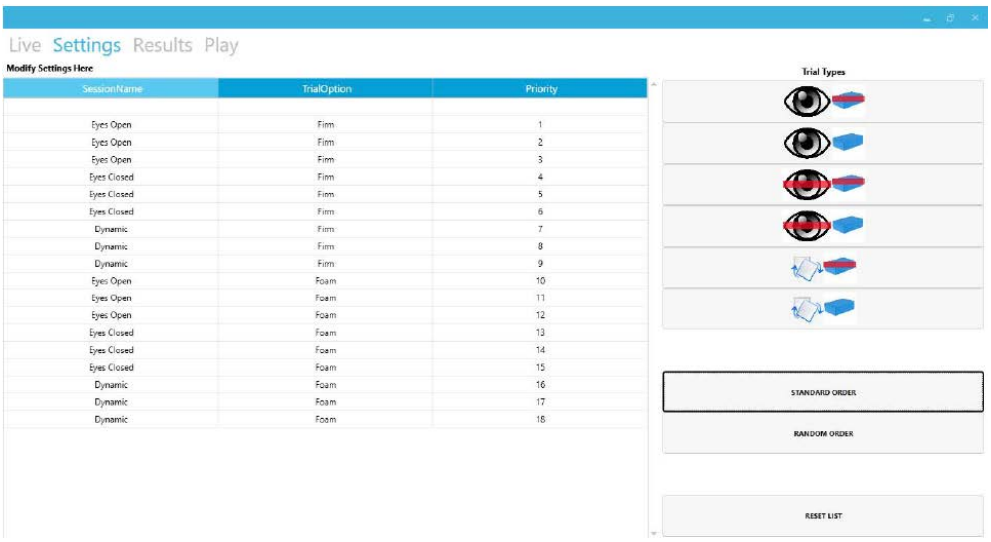

Figure 3.5: Screen shot of the VETS graphic user interface. Testing conditions and order can be selected from this screen. Subject identification, trial length and testing rate in hertz can be designated from a similar screen.

CHAPTER 4:
Results and Discussion

4.1 Overview

Raw data from the VETS device were output into an Excel file for each condition and measurement. These data were compiled into one master Excel file with demographic data added. This provided an easy format to input into statistical software for analysis. Simple statistics on demographic data are provided in the first part of this chapter. Significant results from the analysis of VETS performance measures are presented in the latter half of this chapter. All analyses were conducted using SPSS 19 for Windows. Unless otherwise noted, an alpha level of 0.05 was used to indicate significant effects. SPSS's Descriptive function was used to examine all data for skewness and kurtosis. Variables which were not normally distributed were transformed using the Transform function in SPSS. Mean substitutions were used to replace two instances of missing data.

4.2 Analysis of Demographic

Participants were asked to fill out a demographic survey prior to experimentation. Information given was voluntary with the goal of determining potential confounds. The majority of the participants in this study, 14, were commissioned officers and 1 participant was a Staff Non Commissioned Officer.

4.2.1 Age

The mean age among subjects was 32.9 years (SD = 4.7). The oldest participant was 43 and the youngest was 27, see Figure 4.1.

4.2.2 Gender

Out of the 15 participants, 12 were male and 3 were female.

4.2.3 Service

Three services were represented in this study. Twelve participants were members of the USMC. Two participants were members of the United States Navy (USN). One participant

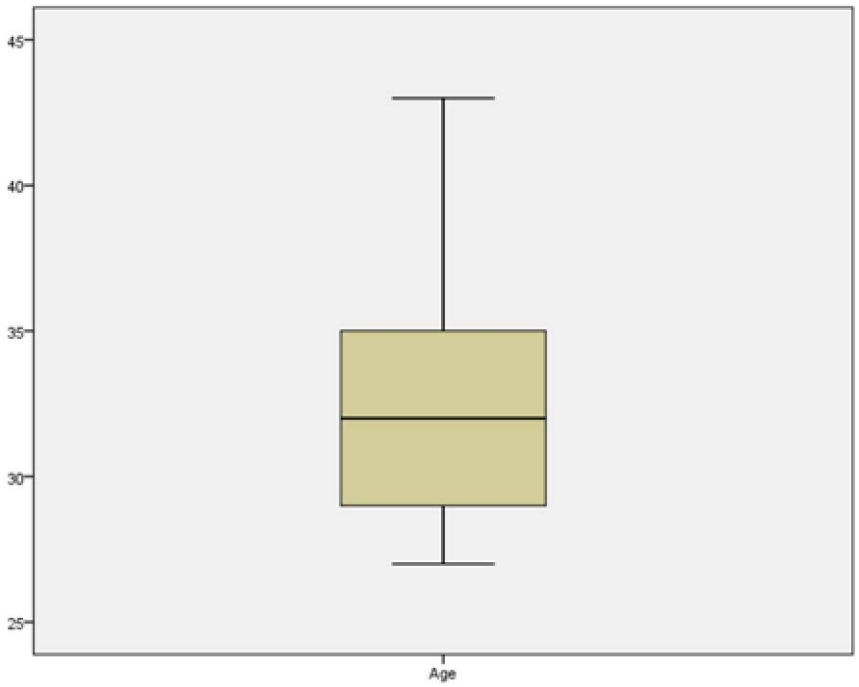

Figure 4.1: Box plot of mean and standard deviation for age of the 15 participants in the Baseline Establishment of Balance using the VETS device study.

was a member of the USA. Participants were at the mid point of their careers with a mean time in service of 11.5 years (*SD* = 4.6), see Figure 4.2.

4.2.4 Height, Weight, and Handedness

The mean height of participants was 69.3 inches (*SD* = 4.2), see Figure 4.3. The mean weight of participants was 182.7 pounds (*SD* = 36.9), 4.3. Two participants were left handed.

4.3 Simulator Sickness Questionnaire Data

There were no significant differences between participants' reported SSQ baseline scores and any of their post-trail scores.

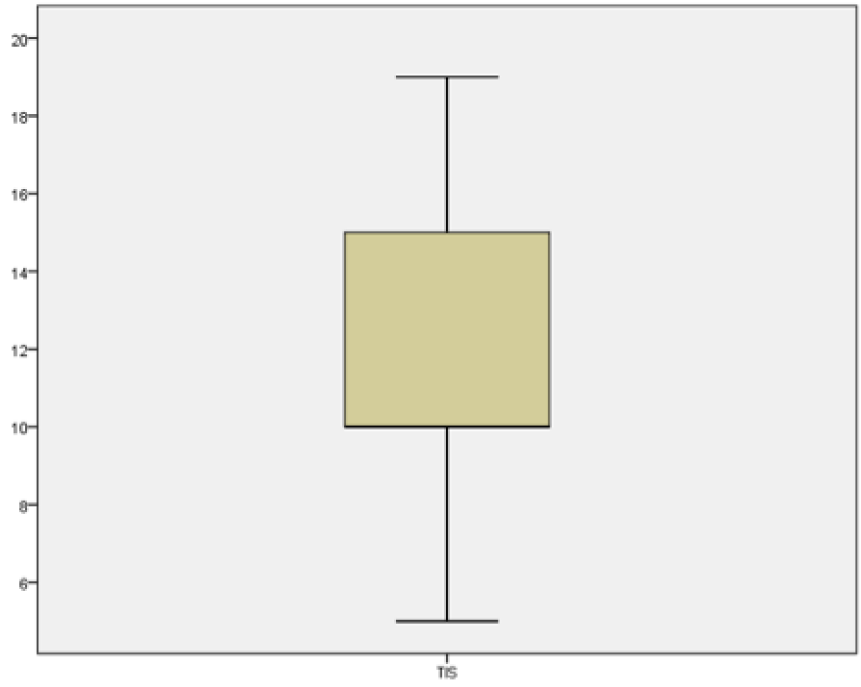

Figure 4.2: Box plot of mean and standard deviation for time in service of the 15 participants in the Baseline Establishment of Balance using the VETS device study.

4.4 Analysis of VETS System Collected Measures

First, a paired-samples t-test was conducted to examine reliability correlations and to compare the means of each VETS performance measure between the first, second and third trial of each session. Next, a one-way repeated measure analysis of variance (ANOVA) was used to examine any differences across testing days within VETS performance measures. Finally, a post-hoc repeated measures ANOVA was performed which examined VETS COP sway and velocity performance measures across both sessions in order to examine differences which existed over time. Means and standard deviations for sway is measured in cm^2, for velocity is measured in cm/sec, and RMS AP and ML are measured in cm. Lower numbers on measurements are considered better postural control while higher number indicate worse postural control.

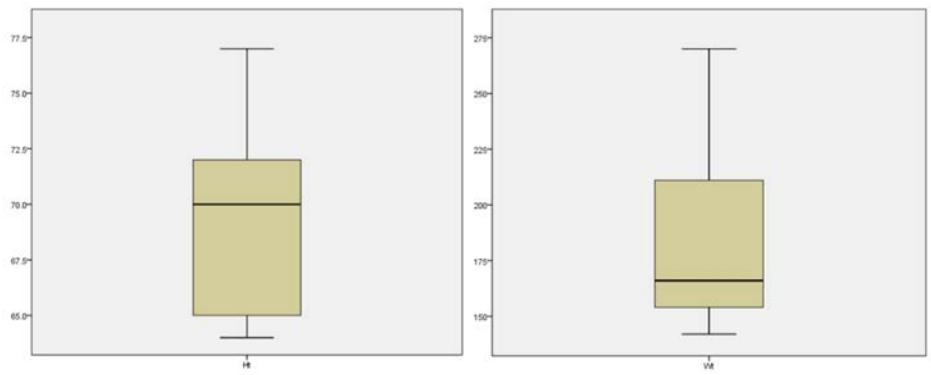

Figure 4.3: The box plot on the left is of mean and standard deviation for height of the 15 participants in the Baseline Establishment of Balance using the VETS device study. The box plot on the right is of mean and standard deviation for weight of the 15 participants in the Baseline Establishment of Balance using the VETS device study.

4.4.1 Paired Samples t-Test Results

A paired-samples t-test was used to compare each of the sway and velocity measures for all conditions by session (first session and second session). Results indicated that most of the variables were not significantly different. However, analysis of the test statistics revealed significant differences between trials for some measures. See Tables 4.1 - 4.12 for results on each sway and velocity measure group. Those with significant differences are indicated with an asterisk (*). Some negative t-values exist in the associated t-test tables, this indicates the direction of the difference in sample means.

4.4.2 Repeated Measures Results

A repeated measures analysis of variance was conducted to assess the differences between the session day (first session or second session) for each VETS performance measure. The repeated measure was each VETS performance measure on the first session and on the second session. Means and standard deviation for sway is measured in cm^2, for velocity is measured in cm/sec, and RMS AP and ML are measured in cm.

Firm Platform Dynamic Scene

Significant differences were found for the firm platform dynamic scene condition of the VETS performance measures between the first and second sessions, see Table 4.13.

Firm Dynamic Center of Pressure Sway

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	4.21	3.20	-.222	.827
Session 1, Trial 2	4.39	3.71		
Session 1, Trial 1	4.21	3.20	.470	.520
Session 1, Trial 3	3.88	2.03		
Session 1, Trial 2	4.39	3.71	.660	.645
Session 1, Trial 3	3.88	2.03		
Session 2, Trial 1	3.25	3.05	-.016	.988
Session 2, Trial 2	3.26	2.09		
Session 2, Trial 1	3.25	3.05	.442	.665
Session 2, Trial 3	3.05	2.90		
Session 2, Trial 2	3.26	2.09	.279	.784
Session 2, Trial 3	3.05	2.90		

Table 4.1: Paired-samples t-test results for Firm Dynamic Center of Pressure Sway.

Firm Dynamic Center of Pressure Velocity

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	2.18	0.49	-.107	.916
Session 1, Trial 2	2.19	0.55		
Session 1, Trial 1	2.18	0.49	.349	.732
Session 1, Trial 3	2.16	0.48		
Session 1, Trial 2	2.19	0.55	.594	.562
Session 1, Trial 3	2.16	0.48		
Session 2, Trial 1	2.07	0.43	-.088	.931
Session 2, Trial 2	2.07	0.34		
Session 2, Trial 1	2.07	0.43	1.37	.192
Session 2, Trial 3	1.97	0.32		
Session 2, Trial 2	2.07	0.34	1.47	.162
Session 2, Trial 3	1.97	0.32		

Table 4.2: Paired-samples t-test results for Firm Dynamic Center of Pressure Velocity.

Firm Eyes Open Center of Pressure Sway

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	4.16	6.86	.997	.366
Session 1, Trial 2	2.56	3.25		
Session 1, Trial 1	4.16	6.86	.887	.390
Session 1, Trial 3	2.76	1.90		
Session 1, Trial 2	2.56	3.25	-.366	.720
Session 1, Trial 3	2.76	1.90		
Session 2, Trial 1	1.65	1.46	-.972	.347
Session 2, Trial 2	2.09	1.66		
Session 2, Trial 1	1.65	1.46	.207	.839
Session 2, Trial 3	1.56	1.07		
Session 2, Trial 2	2.09	1.66	1.28	.222
Session 2, Trial 3	1.56	1.07		

Table 4.3: Paired-samples t-test results for Firm Eyes Closed Center of Pressure Sway.

Firm Eyes Closed Center of Pressure Velocity

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	1.93	0.31	-2.14	.050
Session 1, Trial 2	2.04	0.38		
Session 1, Trial 1	1.93	0.31	-2.88	.012*
Session 1, Trial 3	2.16	0.49		
Session 1, Trial 2	2.04	0.38	-1.21	.247
Session 1, Trial 3	2.16	0.49		
Session 2, Trial 1	1.89	0.33	-.82	.425
Session 2, Trial 2	1.94	0.25		
Session 2, Trial 1	1.89	0.33	-1.44	.173
Session 2, Trial 3	1.99	0.31		
Session 2, Trial 2	1.94	0.25	-1.01	.330
Session 2, Trial 3	1.99	0.31		

Table 4.4: Paired-samples t-test results for Firm Eyes Closed Center of Pressure Velocity.

Firm Eyes Open Center of Pressure Sway

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	4.16	6.86	.997	.366
Session 1, Trial 2	2.56	3.25		
Session 1, Trial 1	4.16	6.86	.887	.390
Session 1, Trial 3	2.76	1.90		
Session 1, Trial 2	2.56	3.25	-.366	.720
Session 1, Trial 3	2.76	1.90		
Session 2, Trial 1	1.65	1.46	-.972	.347
Session 2, Trial 2	2.09	1.66		
Session 2, Trial 1	1.65	1.46	.207	.839
Session 2, Trial 3	1.56	1.07		
Session 2, Trial 2	2.09	1.66	1.28	.222
Session 2, Trial 3	1.56	1.07		

Table 4.5: Paired-samples t-test results for Firm Eyes Open Center of Pressure Sway.

Firm Eyes Open Center of Pressure Velocity

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	1.79	0.35	-.072	.944
Session 1, Trial 2	1.80	0.32		
Session 1, Trial 1	1.79	0.35	-.023	.982
Session 1, Trial 3	1.79	0.24		
Session 1, Trial 2	1.80	0.32	.098	.924
Session 1, Trial 3	1.79	0.24		
Session 2, Trial 1	1.64	0.22	-1.66	.120
Session 2, Trial 2	1.70	0.25		
Session 2, Trial 1	1.64	0.22	-1.64	.123
Session 2, Trial 3	1.68	0.23		
Session 2, Trial 2	1.70	0.25	.723	.481
Session 2, Trial 3	1.68	0.23		

Table 4.6: Paired-samples t-test results for Firm Eyes Open Center of Pressure Velocity.

Foam Dynamic Center of Pressure Sway

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	29.17	13.81	-0.049	.156
Session 1, Trial 2	24.25	13.33		
Session 1, Trial 1	29.17	13.81	-1.295	.002*
Session 1, Trial 3	19.78	37.90		
Session 1, Trial 2	24.25	13.33	-1.185	.164
Session 1, Trial 3	19.78	37.90		
Session 2, Trial 1	18.57	11.71	1.474	.092
Session 2, Trial 2	14.87	7.81		
Session 2, Trial 1	18.57	11.71	1.089	.076
Session 2, Trial 3	14.31	5.98		
Session 2, Trial 2	14.87	7.81	0.139	.622
Session 2, Trial 3	14.31	5.98		

Table 4.7: Paired-samples t-test results for Foam Dynamic Center of Pressure Sway.

Foam Dynamic Center of Pressure Velocity

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	29.17	19.65	1.51	.156
Session 1, Trial 2	24.25	24.87		
Session 1, Trial 1	29.17	19.65	3.84	.002*
Session 1, Trial 3	19.78	16.24		
Session 1, Trial 2	24.25	24.87	1.47	.164
Session 1, Trial 3	19.78	16.24		
Session 2, Trial 1	18.57	12.70	1.81	.092
Session 2, Trial 2	14.87	7.16		
Session 2, Trial 1	18.57	12.70	1.91	.076
Session 2, Trial 3	14.31	7.88		
Session 2, Trial 2	14.87	7.16	.50	.622
Session 2, Trial 3	14.31	7.88		

Table 4.8: Paired-samples t-test results for Foam Dynamic Center of Pressure Velocity.

Foam Eyes Open Center of Pressure Sway

	M	*SD*	*T*	Sig. (2-tailed)
Session 1, Trial 1	4.33	15.00	-.0656	.523
Session 1, Trial 2	4.88	15.00		
Session 1, Trial 1	4.33	15.00	.677	.510
Session 1, Trial 3	3.95	15.00		
Session 1, Trial 2	4.88	15.00	1.762	.100
Session 1, Trial 3	3.95	15.00		
Session 2, Trial 1	6.37	15.00	1.764	.100
Session 2, Trial 2	3.47	15.00		
Session 2, Trial 1	6.37	15.00	1.02	.326
Session 2, Trial 3	4.56	15.00		
Session 2, Trial 2	3.47	15.00	-1.29	.216
Session 2, Trial 3	4.56	15.00		

Table 4.9: Paired-samples t-test results for Foam Eyes Open Center of Pressure Sway.

Foam Eyes Open Center of Pressure Velocity

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	1.99	0.27	-.416	0.683
Session 1, Trial 2	2.02	0.31		
Session 1, Trial 1	1.99	0.27	.774	0.452
Session 1, Trial 3	1.93	0.26		
Session 1, Trial 2	2.02	0.31	1.244	0.234
Session 1, Trial 3	1.93	0.26		
Session 2, Trial 1	2.06	0.53	1.584	0.136
Session 2, Trial 2	1.87	0.21		
Session 2, Trial 1	2.06	0.53	.827	0.422
Session 2, Trial 3	1.94	0.38		
Session 2, Trial 2	1.87	0.21	-.675	0.511
Session 2, Trial 3	1.94	0.38		

Table 4.10: Paired-samples t-test results for Foam Eyes Open Center of Pressure Velocity.

Foam Eyes Closed Center of Pressure Sway

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	19.87	13.81	-.049	.962
Session 1, Trial 2	20.00	13.33		
Session 1, Trial 1	19.87	13.81	-1.3.	.216
Session 1, Trial 3	30.68	37.90		
Session 1, Trial 2	20.00	13.33	-1.19	.256
Session 1, Trial 3	30.68	37.90		
Session 2, Trial 1	17.99	11.71	1.47	.163
Session 2, Trial 2	15.43	7.81		
Session 2, Trial 1	17.99	11.71	.1.01	.295
Session 2, Trial 3	15.21	5.98		
Session 2, Trial 2	15.43	7.81	.14	.891
Session 2, Trial 3	15.21	5.98		

Table 4.11: Paired-samples t-test results for Foam Eyes Closed Center of Pressure Sway.

Firm Platform Blank Scene

Significant differences were found for the firm platform blank scene condition of the VETS performance measures between the first and second sessions, see Table 4.14.

Firm Platform Static Scene

Significant differences were found for the firm platform static scene condition of the VETS performance measures between the first and second sessions, see Table 4.15.

Foam Platform Dynamic Scene

Significant differences were found for the foam platform dynamic scene condition of the VETS performance measures between the first and second sessions, see Table 4.16.

Foam Platform Eyes Closed

Significant differences were found for the foam platform blank scene condition of the VETS performance measures between the first and second sessions, see Table 4.17.

Foam Eyes Closed Center of Pressure Velocity

	M	*SD*	*t*	Sig. (2-tailed)
Session 1, Trial 1	3.98	1.31	.185	.856
Session 1, Trial 2	3.94	1.14		
Session 1, Trial 1	3.98	1.31	.107	.916
Session 1, Trial 3	3.94	1.39		
Session 1, Trial 2	3.94	1.14	-.017	.987
Session 1, Trial 3	3.94	1.39		
Session 2, Trial 1	3.62	0.82	2.22	.043*
Session 2, Trial 2	3.37	0.70		
Session 2, Trial 1	3.62	0.82	2.99	.010*
Session 2, Trial 3	3.20	0.76		
Session 2, Trial 2	3.37	0.70	1.35	.198
Session 2, Trial 3	3.20	0.76		

Table 4.12: Paired-samples t-test results for Foam Eyes Closed Center of Pressure Velocity.

Firm Dynamic Condition				First Session		Second Session	
DV	*F*	*p*	η_p^2	M	SD	M	SD
COP Velocity First Trial	(1, 14)=6.051	0.028	0.302	2.178	0.489	2.068	0.432
COP Velocity Third Trial	(1, 14)=4.925	0.044	0.260	2.157	0.477	1.973	.317
RMS AP Third Trial	(1, 14)=4.686	0.048	0.251	0.545	0.209	0.447	0.138

Table 4.13: Significant results from repeated measure ANOVA between first and second session of the Firm Platform Dynamic Scene.

4.4.3 Velocity and Sway

In an effort to further understand the results presented in Section 4.4.2, a post-hoc repeated-measures ANOVA was performed to examine sway and velocity measures. Figures 4.4 - 4.9 show the profile plots for each sway and velocity measure. All sway measurements are in cm^2 and all velocity measurements are in cm/sec.

4.4.4 Comparison of VETS and SSQ

There are no significant findings from the collection of SSQ data.

Firm Blank Condition				First Session		Second Session	
DV	F	p	η_p^2	M	SD	M	SD
RMS AP First Trial	(1, 14)=4.740	0.047	0.253	0.573	0.277	0.505	0.249
RMS ML Third Trial	(1, 14)=5.406	0.036	0.279	0.319	0.230	0.199	0.082

Table 4.14: Significant results from repeated measure ANOVA between first and second session of the Firm Platform Blank Scene.

Firm Static Condition				First Session		Second Session	
DV	F	p	η_p^2	M	SD	M	SD
COP Sway Third Trial	(1, 14)=10.359	0.006	0.425	2.762	1.897	1.559	1.066
COP Velocity Third Trial	(1, 14)=7.668	0.015	0.354	1.793	0.243	1.681	0.229

Table 4.15: Significant results from repeated measure ANOVA between first and second session of the Firm Platform Static Scene.

Foam Dynamic Condition				First Session		Second Session	
DV	F	p	η_p^2	M	SD	M	SD
COP Sway First Trial	(1, 14)=17.833	0.001	0.560	29.173	19.649	18.574	12.703
COP Sway Third Trial	(1, 14)=4.903	0.044	0.259	19.781	16.237	14.307	7.882
COP Velocity First Trial	(1, 14)=17.296	0.001	0.553	4.848	1.365	4.041	1.184
COP Velocity Second Trial	(1, 14)=8.907	0.010	0.389	4.515	1.932	3.629	0.760
COP Velocity Third Trial	(1, 14)=11.038	0.005	0.441	3.972	1.353	3.465	0.852
RMS ML First Trial	(1, 14)=15.198	0.002	0.521	0.952	0.401	0.769	0.357
RMS AP First Trial	(1, 14)=13.568	0.002	0.492	1.179	0.346	0.976	0.210

Table 4.16: Significant results from repeated measure ANOVA between first and second session of the Foam Platform Dynamic Scene.

Foam Blank Condition				First Session		Second Session	
DV	F	p	η_p^2	M	SD	M	SD
COP Velocity Second Trial	(1, 14)=17.672	0.001	0.558	3.939	1.144	3.366	0.697
COP Velocity Thrid Trial	(1, 14)=8.461	0.011	0.377	3.944	1.386	3.201	0.764

Table 4.17: Significant results from repeated measure ANOVA between first and second session of the Foam Platform Blank Scene.

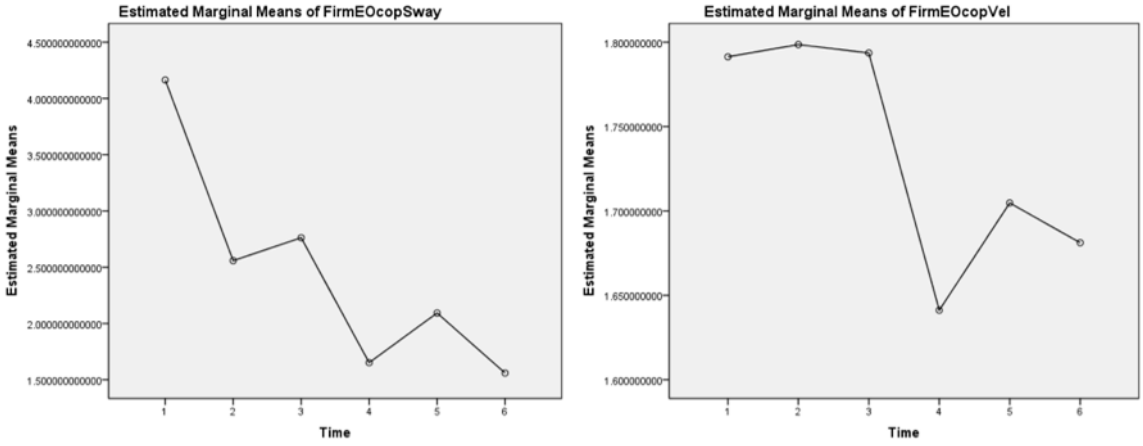

Figure 4.4: Both graphs represent the mean of measurements taken for each trial of each session in the Firm Platform Static Scene. Data points are in chronological order, the first three points were taken during the first session and the last three points were taken during the second session. The graph on the left represents Sway area in cm^2 and the graph on the right represents Velocity in cm/sec.

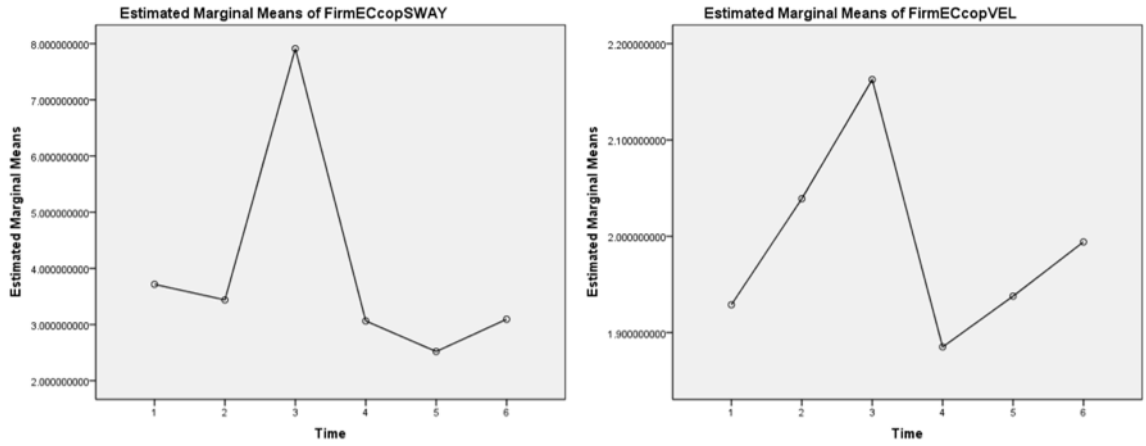

Figure 4.5: Both graphs represent the mean of measurements taken for each trial of each session in the Firm Platform Blank Scene. Data points are in chronological order, the first three points were taken during the first session and the last three points were taken during the second session. The graph on the left represents Sway area in cm^2 and the graph on the right represents Velocity in cm/sec.

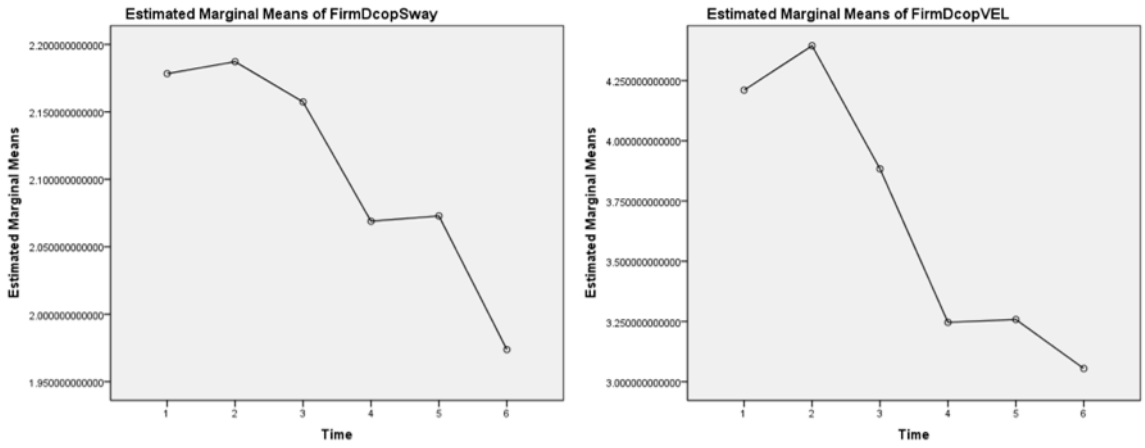

Figure 4.6: Both graphs represent the mean of measurements taken for each trial of each session in the Firm Platform Dynamic Scene. Data points are in chronological order, the first three points were taken during the first session and the last three points were taken during the second session. The graph on the left represents Sway area in cm^2 and the graph on the right represents Velocity in cm/sec.

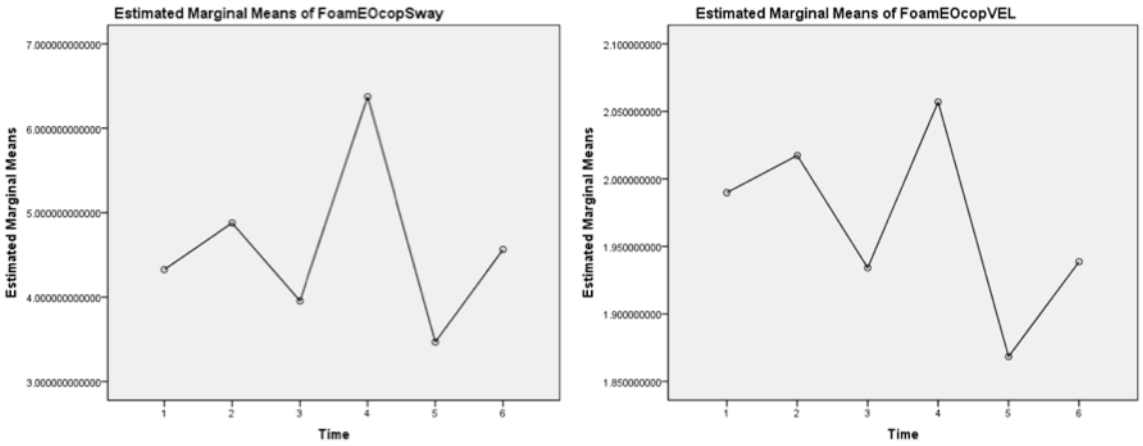

Figure 4.7: Both graphs represent the mean of measurements taken for each trial of each session in the Foam Platform Static Scene. Data points are in chronological order, the first three points were taken during the first session and the last three points were taken during the second session. The graph on the left represents Sway area in cm^2 and the graph on the right represents Velocity in cm/sec.

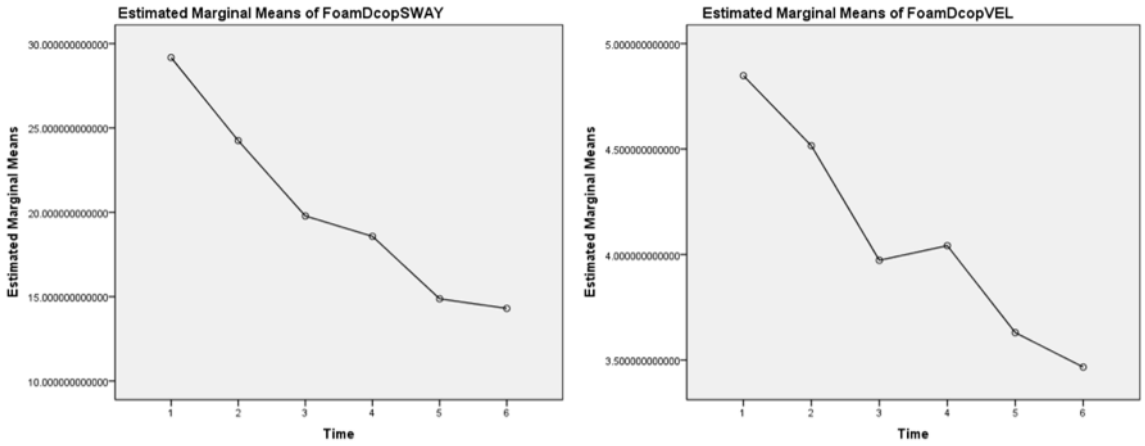

Figure 4.8: Both graphs represent the mean of measurements taken for each trial of each session in the Foam Platform Dynamic Scene. Data points are in chronological order, the first three points were taken during the first session and the last three points were taken during the second session. The graph on the left represents Sway area in cm^2 and the graph on the right represents Velocity in cm/sec.

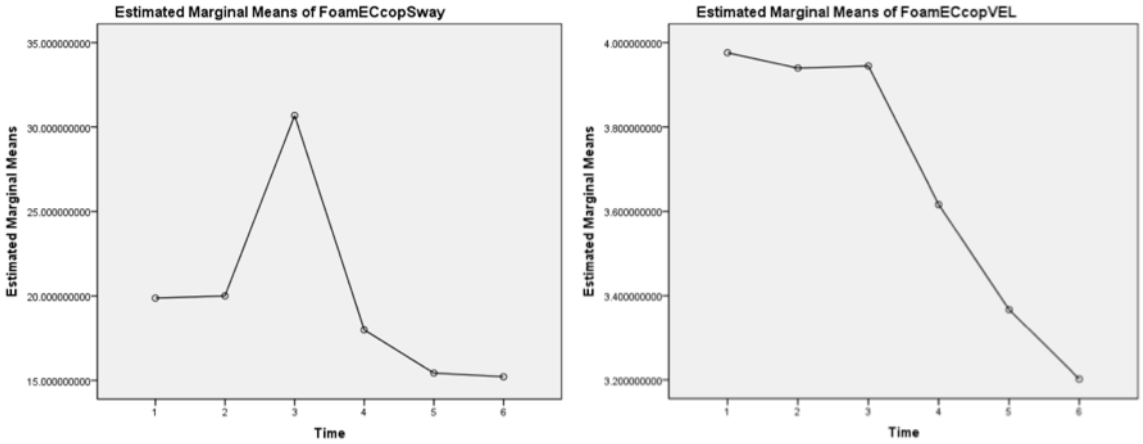

Figure 4.9: Both graphs represent the mean of measurements taken for each trial of each session in the Foam Platform Blank Scene. Data points are in chronological order, the first three points were taken during the first session and the last three points were taken during the second session. The graph on the left represents Sway area in cm^2 and the graph on the right represents Velocity in cm/sec.

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CHAPTER 5:
Discussion and Recommendations

5.1 Discussion

5.1.1 VETS

No adverse simulator sickness effects were experienced during this research. Data gathered through the use of SSQ during the course of this study suggests that the use of a VE does not adversely affect an individual's performance during or after the test.

5.1.2 VETS as a mTBI screening device for expeditionary forces

Evidence from the paired samples t-test support the use of a WBB with the VETS software suite as a reliable measure of dependent variables that assess postural control. Results from the repeated measures ANOVA support the use of VETS system to reliably measures postural control variables of interest (center of pressure sway and velocity) in a healthy military population. Where statistically significant results where noted, a trend towards better performance during the second session was noted, see Figures 4.4 - 4.9. This trend toward increased postural control during the second session could be an indicator of a practice effect experienced by subjects. If a practice effect is being seen, care should be taken when comparing multiple sessions in a healthy population to that of concussed individuals. These results contribute evidence that supports the use of the VETS system as a measure of postural control in deployed environments, which can be used as a tool to assist clinicians determine the possible presence of a TBI.

Initial results from data collection of concussed individuals, in a separate study, show a two to three fold difference in mean scores (trending toward worse balance in concussed individuals) from the healthy population scores collected in this study. This could indicate that a significant change index can be determined between healthy and concussed individuals which further supports the use of the VETS device as a tool for TBI screening.

Low cost, ease of set up and use, real-time results, and quantitative measurements are favorable factors of the VETS device for use as a tool by expeditionary forces. Components

of this system can be further reduced by using existing computers and TV screens already present in a deployed environment. The need for a dedicated computer and TV screen may not be necessary in most instances and these already present components may provide multiple uses to deployed units. About five to six VETS devices can be purchased at a cost of about three thousand dollars for the WBB, Airex foam pad, computer, and TV for the price the average clinical grade force plate on the market today. The TV component is by far the most expensive and, as stated, may already be available for use in a deployed unit.

5.2 Recommendations

5.2.1 Recommendations for Naval Leadership

The positive attributes of the VETS device warrant further support from Naval Leadership interested in arming medical providers with useful tools for the detection of a TBI. A low cost quantitative screening device for TBI is feasible with today's technology, but it requires further investigation to support its validity. Though the use of this device on ship will likely be infeasible due to an inherent unstable platform, the USN has a large presence stationed abroad at land based activities who would likely benefit from such a tool. The USMC, with medical services provided by the USN, the USA, and SOCOM would benefit most from having a screening tool such as this to use in remote deployed environments for personnel engaged in combat operations. Especially at the small unit level where robust medical capabilities may be geographically distant. The United States Air Force (USAF) could use this tool in their medical service corps and with their expeditionary personnel supporting ground operations abroad. Though significant benefit lies in the deployed realm, use of a tool such as the VETS device should not be limited to deployed personnel. Having these devices at home station clinics and hospitals might also be of great use. Advantages of such a device are not limited to Naval expeditionary forces.

5.2.2 Recommendations for Future Research

There are many opportunities for future research associated with this topic. Since the WBB is a recreational device, not a clinical grade force plate, the reliability and consistency of measurements between multiple WBB should be tested to ensure quality among devices. Potential exists in investigating the feasibility of recording baseline scores for individuals to be compared later in the event of an injury vice using healthy norms. Additionally, gather-

ing more data from a healthy population would strengthen statistical power for determining reliability of the test and provide additional data to investigate the potential practice effect noted in this study.

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APPENDIX A:
Military Acute Concussion Evaluation

Concussion evaluation, Military Acute Concussion Evaluation, currently in use by military medical providers, from [41].

MACE
Military Acute Concussion Evaluation

DVBIC Defense and Veterans Brain Injury Center

Defense Centers of Excellence for Psychological Health & Traumatic Brain Injury

Patient Name: _____

Service Member ID#: _____ Unit: _____

Date of Injury: _____ Time of Injury: _____

Examiner: _____

Date of Evaluation: _____ Time of Evaluation: _____

CONCUSSION SCREENING

Complete this section to determine if there was both an injury event AND an alteration of consciousness.

1. Description of Incident

A. Record the event as described by the service member or witness.

Use open-ended questions to get as much detail as possible.

_____

_____

_____

_____

Key questions:

- Can you tell me what you remember?
- What happened?

B. Record the type of event.

Check all that apply:

☐ Explosion/Blast ☐ Fragment ☐ Motor Vehicle Crash

☐ Blunt Object ☐ Sports Injury ☐ Gunshot Wound

☐ Fall ☐ Other _____

C. Was there a head injury event?

☐ **YES** ☐ **NO**

Key questions:

- Did your head hit any objects?
- Did any objects strike your head?
- Did you feel a blast wave? (A blast wave that is felt striking the body/head is considered a blow to the head.)

CONCUSSION SCREENING – continued

2. Alteration of Consciousness or Memory (AOC/LOC/PTA)

A. Was there Alteration of Consciousness (AOC)?
AOC is temporary confusion or "having your bell rung."

☐ YES ☐ NO

If yes, for how long? ____ minutes

Key question:
- Were you dazed, confused, or did you "see stars" immediately after the injury?

B. Was there Loss of Consciousness (LOC)?
LOC is temporarily passing out or blacking out.

☐ YES ☐ NO

If yes, for how long? ____ minutes

Key question:
- Did you pass out or black out?

C. Was there any Post Traumatic Amnesia (PTA)?
PTA is a problem remembering part or all of the injury events.

☐ YES ☐ NO

If yes, for how long? ____ minutes

Key questions:
- What is the last thing you remember before the event?
- What is the first thing you remember after the event?

D. Was there a witness?

☐ YES ☐ NO

If yes, name of witness: _____

Tips for assessment:
- Ask witness to verify AOC/LOC/PTA and estimate duration.

CONCUSSION SCREENING RESULTS (Possible Concussion?)

YES to 1C
AND
YES to 2A, 2B *or* 2C

CONTINUE the MACE:
- Complete the Cognitive, Neurological and Symptoms portions of the MACE

NO to 1C
OR
NO to 2A, 2B *and* 2C

STOP the MACE:
- Evaluate and treat any other injuries or symptoms
- Enter negative screening result into electronic medical record (V80.01)
- Communicate results with provider and line commanders
- Check for history of previous concussions and refer to Concussion Management Algorithm for appropriate rest period

COGNITIVE EXAM[a]

3. Orientation

Score 1 point for each correct response.

Ask This Question	Incorrect	Correct
"What month is this?"	0	1
"What is the date or day of the month?"	0	1
"What day of the week is it?"	0	1
"What year is it?"	0	1
"What time do you think it is?"	0	1
Correct response must be within 1 hour of actual time.		

ORIENTATION TOTAL SCORE ____/5

4. Immediate Memory

Choose one list (A-F below) and use that list for the remainder of the MACE.

Read the script for each trial and then read all 5 words. Circle the response for each word for each trial. Repeat the trial 3 times, even if the service member scores perfectly on any of the trials.

Trial 1 Script:

- "I am going to test your memory. I will read you a list of words and when I am done, repeat back to me as many words as you can remember, in any order."

Trials 2 and 3 Script:

- "I am going to repeat that list again. Repeat back to me as many words as you can remember, in any order, even if you said them before."

	Trial 1		Trial 2		Trial 3	
List F	Incorrect	Correct	Incorrect	Correct	Incorrect	Correct
Dollar	0	1	0	1	0	1
Honey	0	1	0	1	0	1
Mirror	0	1	0	1	0	1
Saddle	0	1	0	1	0	1
Anchor	0	1	0	1	0	1

IMMEDIATE MEMORY TOTAL SCORE ____/15

Immediate Memory Alternate Word Lists

List E	List D	List C	List B	List A
Jacket	Finger	Baby	Candle	Elbow
Arrow	Penny	Monkey	Paper	Apple
Pepper	Blanket	Perfume	Sugar	Carpet
Cotton	Lemon	Sunset	Sandwich	Saddle
Movie	Insect	Iron	Wagon	Bubble

NEUROLOGICAL EXAM

5. Eyes

Test pupil response to light, tracking

☐ Normal

☐ Abnormal

Tips for assessment:

- Pupils should be round, equal in size and briskly constrict to a direct, bright light.
- Both eyes should smoothly track your finger side-to-side and up and down.

6. Speech

Test speech fluency and word finding

☐ Normal

☐ Abnormal

Tips for assessment:

- Speech should be fluid and effortless – no pauses or unnatural breaks.
- Assess difficulties with word finding:
  - Does service member have trouble coming up with the name of a common object?

7. Motor

Test grip strength and pronator drift

☐ Normal

☐ Abnormal

Tips for assessment:

- Assess grip strength.
- Assess for pronator drift for 5-10 seconds by directing patient to close eyes and extend arms forward, parallel to the ground with palms up:
  - Does either palm turn inward?
  - Does either arm drift down?

8. Balance

Tandem Romberg Test

☐ Normal

☐ Abnormal

Tips for assessment:

- Have patient stand with eyes closed, one foot in front of the other heel-to-toe, arms extended forward, palms up. Observe for 5-10 seconds:
  - Does the service member stumble or shift feet?

NEUROLOGICAL EXAM RESULTS

☐ All Normal **Green**

☐ Any Abnormal **Red**

COGNITIVE EXAM[a] - Continued

9. Concentration

A. Reverse Digits

Read the script and begin the trial by reading the first string of numbers in Trial 1.

Script:

- "I am going to read you a string of numbers. When I am finished, repeat them back to me backward. That is, in reverse order of how I read them to you. For example, if I said 7 - 1 - 9, then you would say 9 - 1 - 7."

Circle the response for each string.

- If correct on string length of Trial 1, proceed to the next longer string length in the same column.
- If incorrect on string length of Trial 1, move to the same string length of Trial 2.
- If incorrect on both string lengths in Trials 1 and 2, **STOP** and record score as zero for that string length. Record total score as sum of previous correct trials.

List F			
Trial 1	**Trial 2** (if Trial 1 is incorrect)	**Incorrect**	**Correct**
2-7-1	4-7-9	**0**	**1**
1-6-8-3	3-9-2-4	**0**	**1**
2-4-7-5-8	8-3-9-6-4	**0**	**1**
5-8-6-2-4-9	3-1-7-8-2-6	**0**	**1**

REVERSE DIGITS SCORE (9A) ____/4

Concentration Alternate Number Lists

Note: Use the same list (A-F) that was used in Question 4.

List E	
Trial 1	**Trial 2**
3-8-2	5-1-8
2-7-9-3	2-1-6-9
4-1-8-6-9	9-4-1-7-5
6-9-7-3-8-2	4-2-7-9-3-8

List D	
Trial 1	**Trial 2**
7-8-2	9-2-6
4-1-8-3	9-7-2-3
1-7-9-2-6	4-1-7-5-2
2-6-4-8-1-7	8-4-1-9-3-5

List C	
Trial 1	**Trial 2**
1-4-2	6-5-8
6-8-3-1	3-4-8-1
4-9-1-5-3	6-8-2-5-1
3-7-6-5-1-9	9-2-6-5-1-4

List B	
Trial 1	**Trial 2**
5-2-6	4-1-5
1-7-9-5	4-9-6-8
4-8-5-2-7	6-1-8-4-3
8-3-1-9-6-4	7-2-7-8-5-6

List A	
Trial 1	**Trial 2**
4-9-3	6-2-9
3-8-1-4	3-2-7-9
6-2-9-7-1	1-5-2-8-5
7-1-8-4-6-3	5-3-9-1-4-8

COGNITIVE EXAM[a] - Continued

9. Concentration - Continued

B. Months in Reverse Order

Script:

- "Now tell me the months of the year in reverse order. Start with the last month and go backward. So you'll say: December, November…Go ahead."

Correct Response:
Dec – Nov – Oct – Sep – Aug – Jul – Jun – May – Apr – Mar – Feb – Jan

	Incorrect	Correct
ALL months in reverse order	0	1

MONTHS IN REVERSE ORDER (9B) ____/1

CONCENTRATION TOTAL SCORE ____/5

Sum of scores:
9A (0-4 points) and 9B (0 or 1 point)

10. Delayed Recall

Read the script and circle the response for each word.
Do NOT repeat the word list.

Note: Use the same list (A-F) that was used in Question 4.

Script:

- "Do you remember that list of words I read a few minutes earlier? I want you to tell me as many words from that list as you can remember. You can say them in any order."

List F	Incorrect	Correct
Dollar	0	1
Honey	0	1
Mirror	0	1
Saddle	0	1
Anchor	0	1

DELAYED RECALL TOTAL SCORE ____/5

Delayed Recall Alternate Word Lists

List E	List D	List C	List B	List A
Jacket	Finger	Baby	Candle	Elbow
Arrow	Penny	Monkey	Paper	Apple
Pepper	Blanket	Perfume	Sugar	Carpet
Cotton	Lemon	Sunset	Sandwich	Saddle
Movie	Insect	Iron	Wagon	Bubble

SYMPTOM SCREENING

11. Symptoms — Check all that apply:

- ☐ Headache
- ☐ Balance Problems
- ☐ Irritability
- ☐ Dizziness
- ☐ Nausea/Vomiting
- ☐ Visual Disturbances
- ☐ Memory Problems
- ☐ Difficulty Concentrating
- ☐ Ringing in the Ears
- ☐ Other _____

SUMMARY

Record the data for correct MACE documentation.

Cognitive Summary

Orientation Total Score - Q3	___/5
Immediate Memory Total Score (all 3 trials) **- Q4**	___/15
Concentration Total Score (Sections A and B) **- Q9**	___/5
Delayed Recall Total Score - Q10	___/5
COGNITIVE RESULTS	___/30

NEUROLOGICAL RESULTS (Page 4)

- ☐ Normal **(Green)**
- ☐ Abnormal **(Red)**

SYMPTOM RESULTS

- ☐ No symptoms **(A)**
- ☐ 1 or more symptoms **(B)**

MACE RESULTS (Report all 3 parts.) Example: 24/Red/B

Abnormality in any area should be discussed with provider.

C _____ **Cognitive** / **N** _____ **Neurological** / **S** _____ **Symptoms**

CONCUSSION HISTORY IN PAST 12 MONTHS

12. During the past 12 months have you been diagnosed with a concussion, not counting this event?

☐ **YES** ☐ **NO**

If yes, how many? _____

Refer to Concussion Management Algorithm for clinical care guidance.

ADDITIONAL INFORMATION ABOUT MACE COGNITIVE SCORES

Although cognitive is listed first in the summary of MACE results, this should not suggest that any one of the three screening categories is more or less important than the others. Each area (Cognitive, Neurological, Symptoms) must be evaluated carefully. The results of all three evaluations must be included in any MACE report for it to be considered complete.

Regarding cognitive scores, in studies of non-concussed subjects, the mean total cognitive score was 28. Therefore, a score of < 30 does not imply that a concussion has occurred. Definitive normative data for a cut-off score are not available. The Concussion Management Algorithm stipulates that a cognitive score of < 25 or the presence of symptoms requires consultation with a provider.

Repeating the MACE cognitive exam with a different version (A-F) may be used to evaluate acute concussion recovery; however, a physical exam and symptom assessment must accompany any repeated cognitive exam. Providers should be mindful of other factors affecting the MACE cognitive score such as sleep deprivation, medications or pain.

Coding Tips for Concussion:

1. Primary code (corpsmen/medics require co-sign)
   - 850.0 – Concussion without LOC
   - 850.11 – Concussion with LOC ≤ 30 min.
2. Personal history of TBI in Global War on Terror (GWOT)
   - V15.52_2 – Injury related to GWOT, mild TBI
3. Symptom codes
   - As appropriate
4. Deployment status code
   - V70.5_5 – During deployment encounter
5. Screening code
   - V80.01 – Special screening for TBI code
6. E-code (external cause of injury)
   - E979.2 (if applicable) – Terrorism involving explosions and fragments

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APPENDIX B:
Institutional Review Board Approval

Naval Postgraduate School
Human Research Protection Program

From: President, Naval Postgraduate School (NPS)
To: LT Lee Sciarini, USN
Dr. Joe Sullivan
Maj Casey DeMunck, USMC
Via: Chairman, Institutional Review Board (IRB)

Subj: BASELINE ESTABLISHMENT USING VIRTUAL ENVIRONMENT TBI SCREENING (VETS)

Encl: (1) Approved IRB Initial Review Protocol

1. The NPS IRB is pleased to inform you that the NPS President has approved your initial review protocol (NPS IRB# NPS.2015.0030-IR-EP7-A). The approved IRB Protocol is found in enclosure (1). Completion of the CITI Research Ethics Training has been confirmed.

2. This approval expires on 30 June 2015. If additional time is required to complete the research, a continuing review report must be approved by the IRB and NPS President prior to the expiration of approval. At expiration all research (subject recruitment, data collection, analysis of data containing PII) must cease.

3. You are required to obtain documented consent according to the attached approved consent procedure.

4. You are required to report to the IRB any unanticipated problems or serious adverse events to the NPS IRB within 24 hours of the occurrence.

5. Any proposed changes in IRB approved research must be reviewed and approved by the NPS IRB and NPS President prior to implementation except where necessary to eliminate apparent immediate hazards to research participants and subjects.

6. As the Principal Investigator (PI) it is your responsibility to ensure that the research and the actions of all project personnel involved in conducting this study will conform with the IRB approved protocol and IRB requirements/policies.

Subj: BASELINE ESTABLISHMENT USING VIRTUAL ENVIRONMENT TBI SCREENING (VETS)

7. At completion of the research, no later than expiration of approval, the PI will close the protocol by submitting an End of Experiment Report.

Lawrence G. Shattuck, PhD
Chair
Institutional Review Board

Ronald A. Route
Vice Admiral, U.S. Navy (Ret.)
President, Naval Postgraduate School

Date: 3-12-2015

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APPENDIX C:
Recruitment Flyer

Test Your Balance for TBI Research

Volunteers Needed to Help Traumatic Brain Injury (TBI) Research

Come take part in a study that aims to use balance as a screening tool for concussion/TBI. Results from this study will benefit TBI research for developing simple tools to test for concussion in deployed environments.

No experience with a Wii Balance Board or with Virtual Environments is needed. During this study, you will be asked to stand on a Wii Balance Board while viewing a VE on a large screen television. Various scenes will be presented, each lasting 30 seconds with a short rest time in between. You will also be asked to fill out a short demographics survey and simulator sickness questionnaire. The purpose of this study is to demonstrate the validity and reliability of a portable, deployable system that can be used to assist with assessment of concussion in austere environments. Specifically, the VETS device will be utilized to collect baseline balance data on a healthy military population.

WHO: U.S. Military personnel.
WHERE: Watkins 212A
HOW LONG: Approximately 30 mins.
WHEN: During normal school hours.
HOW: Contact Casey DeMunck at cgdemunc@nps.edu to schedule.

Risks associated with this study are negligible. Your participation is completely voluntary and confidential. The principal investigator for this study is LT Lee Sciarini (lwsciari@nps.edu). Please contact the NPS IRB Chair Dr. Larry Shattuck (lgshattu@nps.edu) with any questions regarding your rights as a participant.

APPENDIX D:
Simulator Sickness Questionnaire

No_____ Date_____

SIMULATOR SICKNESS QUESTIONNAIRE

Kennedy, Lane, Berbaum, & Lilienthal (1993)***

Instructions : Circle how much each symptom below is affecting you right now.

1. General discomfort	None	Slight	Moderate	Severe
2. Fatigue	None	Slight	Moderate	Severe
3. Headache	None	Slight	Moderate	Severe
4. Eye strain	None	Slight	Moderate	Severe
5. Difficulty focusing	None	Slight	Moderate	Severe
6. Salivation increasing	None	Slight	Moderate	Severe
7. Sweating	None	Slight	Moderate	Severe
8. Nausea	None	Slight	Moderate	Severe
9. Difficulty concentrating	None	Slight	Moderate	Severe
10. « Fullness of the Head »	None	Slight	Moderate	Severe
11. Blurred vision	None	Slight	Moderate	Severe
12. Dizziness with eyes open	None	Slight	Moderate	Severe
13. Dizziness with eyes closed	None	Slight	Moderate	Severe
14. *Vertigo	None	Slight	Moderate	Severe
15. **Stomach awareness	None	Slight	Moderate	Severe
16. Burping	None	Slight	Moderate	Severe

* Vertigo is experienced as loss of orientation with respect to vertical upright.

** Stomach awareness is usually used to indicate a feeling of discomfort which is just short of nausea.

Last version : March 2013

***Original version : Kennedy, R.S., Lane, N.E., Berbaum, K.S., & Lilienthal, M.G. (1993). Simulator Sickness Questionnaire: An enhanced method for quantifying simulator sickness. *International Journal of Aviation Psychology, 3*(3), 203-220.

APPENDIX E:
Demographics Survey

Virtual Environment Traumatic Brain Injury Screen (VETS) Study
Demographic Survey

Subject#: Date:

Please provide the following information. You may use the back of this page or request additional paper if needed.

1. Age: _____

2. Gender: Male ____ Female ____

3. What is your preferred hand for writing? Right ____ Left ____

4. Do you serve or have you served in any armed forces? Yes ____ No ____

4a. If yes, Branch: _____ Rank: _____ Years: _____

5. What is your rating/MOS/career field? For example: Surface Warfare Officer, pilot, infantry officer, etc.

5a. MOS/rating (0402, 1802, 3002, etc): _____

5b. In plain English (Pilot, Yeoman, Armor, etc) _____

6. Have you been deployed overseas? (May include non-combat deployments)

Yes ____ No ____

6a. If YES, date of return from most recent deployment: _____

6b. Location of most recent deployment: _____

6c. Main responsibilities during most recent deployment: _____

7. Have you been diagnosed with a concussion/TBI? Yes____ No____

7a. If so, approximately how long ago: _____

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Appendix 9

Title: “Effects of concussion recovery phase on symptom provocation using vestibular and ocular motor assessments”

Cheever K[3], McDevitt J[1,4], Tierney RT[3], Wright WG[1,2,*]

[1]Department of Physical Therapy, Temple University, Philadelphia, PA USA
[2]Department of Bioengineering, Temple University, Philadelphia, PA USA
[3]Department of Kinesiology, Temple University, Philadelphia, PA USA
[4]Department of Athletic Training, East Stroudsburg University, East Stroudsburg, PA USA

*Corresponding author:
W. Geoffrey Wright, PhD
wrightw@temple.edu

Key words: near point convergence, optokinetic stimulation, concussion, virtual reality, posture

DRAFT

Background: Ocular-motor testing is quickly emerging as a valuable component of the diagnostic portion of a sport concussion assessment when combined with symptom scores. However, the usefulness of ocular-motor testing in helping to track recovery following a sports related concussion and aid in return to play decisions remains unclear.

Purpose: To evaluate the usefulness of several readily available oculomotor and vestibular tests for assessing S/S from injury and tracking recovery from a sport related concussion.

Materials and methods: Participants were divided into 3 groups: healthy controls (n=58), acute concussion (n=21) and post-concussion (n=10). The acute concussion group suffered a concussion ≤9 days prior to initial assessment, while the prolonged recovery group suffered a concussion ≥16 days prior to initial assessment. Repeated measures ANOVA compared initial, 2 week and 6-week follow-up values between groups. Follow-up logistic equation to determine the accuracy of the diagnostic protocol.

Results: Statistically significant differences in provoked symptoms between acutely concussed group and healthy participants at baseline were observed for the GST, REH, SPS, SPF, and OKN and total combined number of symptoms. NPC was higher in the acutely concussed group (5.4±2.8cm) compared to the healthy control group (3.4±1.9cm). Changes across time showed REH symptoms improved after 2 weeks in the acute group only; GST and SPS symptoms showed no change across time; SPF symptoms improved after 2 weeks (p=.024) and 6 weeks (p=.038) in the acute group, with no other changes across time observed; OKN symptoms improved after 2 weeks (p=.027) and 6 weeks (p=.041).

Conclusions: Ocular motor tests such as near point of convergence as well as symptom provocation following the Horizontal Gaze-Stabilization Test (GST) and Rapid Eye Horizontal Test (REH) appear to be 91% sensitive to the effects of a concussion. Additionally, they appear to give valuable insight during the recovery process that may give clinicians added information when making return to play decisions and tracking recovery following a sport related concussion. Given the limited equipment, training and small time requirement, ocular-motor tests such as near point of convergence, GST, REH are valuable additions to a concussion evaluation protocol.

INTRODUCTION

Despite the recent increase in awareness about potential cumulative effects of repeated head impacts, an estimated one third of all concussions remain undiagnosed.[1] Moreover, a study of 730 NCAA Division I football athletes found that during a football player's career they experience nearly three undiagnosed concussions and over a dozen collisions, which lead to one or more symptoms.[2] The subjectivity and variance of self-reported symptoms combined with a general lack of objective diagnostic criteria complicate efforts to accurately identify a concussion.[3-5] In order to overcome the obstacles faced in concussion diagnosis, trends in concussion management suggest a multifaceted approach including not only a signs and symptoms (S/S) evaluation but the inclusion of ocular-motor, cervical, and vestibular screenings.[6-9] A recent study we conducted suggested that a clinical evaluation that incorporated advanced posture control analysis and oculomotor assessment can discriminate between a concussed athlete and healthy controls with 98.6% accuracy.[9] This supports other reports, which show incorporating a brief vestibular and ocular motor screening increases the probability of detecting a concussion by 50%.[9] However, the extent to which these test detect individuals suffering from prolonged recovery, and aid in return to play decisions is relatively unknown.

DRAFT

Many diagnostic tests have been proposed and show potential to reliably detect deficits in postural control in a concussed population.[9-11] More common tests include the Balance Error Scoring System (BESS) and instrumented balance exams such as the Sensory Organization Test (SOT),[12-13] while others include advanced technology such as the use of virtual reality.[12,14,15] Objective outcome measures with high sensitivity and specificity often require costly instruments such as high resolution cameras and force plates that are not readily available. Futhermore, clinically-oriented balance tests such as the SOT, which examines the integration of vestibular, visual, and somatosensory inputs during postural maintenance are not able to be on a sideline. This lack of accessibility has led researchers to look at the potential sensitivity of additional expedient and accessible clinical testing that targets alterations in cognition,[16,17] oculomotor function,[18-19] and/or vestibular function.[8,9]

Feasibility, accessibility and validity are three of the primary concerns when considering the recommendation of any assessment tool.[20] As self-reported symptoms are generally the first indication of a concussion, the purpose of this study was to evaluate the usefulness of several readily available oculomotor and vestibular tests for assessing S/S from injury and tracking recovery from concussion. Because tracking the timeline of recovery is essential for clinical management, each test was performed at 2 weeks and 6 weeks post initial evaluation. The proposed multifaceted approach will allow clinicians to detect deficits in vestibular and/or oculomotor structures following a head impact allowing for targeted diagnosis and treatment.

METHODS

Study design

DRAFT

A repeated measures research design with a known-groups approach (i.e. healthy vs concussion vs. prolonged recovery) was implemented to determine the best clinical assessment. Group 1 consisted of healthy participants free from any head, vestibular, ocular and/or lower extremity injury in the previous 6 months. Group 2 (acute) included participants who had recently (≤10 days) suffered a concussion diagnosed by a health care professional. Group 3 prolonged recovery from post-concussive symptoms (PCS) consisted of participants who had self-reported suffering a concussion in the previous 6 months and continued to suffer from one or more symptoms of a concussion >14 days post initial injury. Follow-up assessments were completed at 2 weeks and 6 weeks following the initial evaluation in all three groups.

Subjects

A total of 89 active college students participating in either a Division I NCAA sport or college club sport volunteered to participate in this study (48 males; 41 females). There were 58 healthy control participants (21.7±3.5 years; 173.2±9.4cm; 71.4±12.2kg), 21 concussed (20.5±2.3 years; 174.4±10.7cm; 72.8±8.4kg) and 10 prolonged PCS (20.5±2.7 years; 178.3±9.9cm; 75.1±8kg). The acute group had experienced symptoms for 3-10 days, while the prolonged recovery athletes had experienced symptoms for 16-120 days post injury. Concussion in this study was defined as sustaining a pathomechanical event that induced one or more concussion S/S diagnosed by a health care provider.[7,21] Participants in the prolonged recovery group self-reported having suffered a concussion in the previous 6 months, and were currently suffering from self-reported symptoms at the time of the initial evaluation.

Instrumentation

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The dependent variable for each of the four symptom-oriented clinical tests that were administered was a 7-point verbal rating scale (VRS) used to report dizziness, headache, and nausea ("No symptoms"=0, the highest level of symptoms=6). Each participant was asked to rate his or her level of dizziness, headache, and nausea from 0-6 prior to clinical testing to establish a baseline symptom severity score. They were asked to rate the same symptoms immediately following each test using the 7-point VRS. The within-subject change from baseline level was used as the outcome measure in the statistical analysis. Following each test, scores were summed across each of the three symptoms (maximum score 18) as the number of symptoms provoked.

Symptom Oriented Clinical Testing

The following clinical tests were performed following the methodology previously described by McDevitt et al.[9] for rapid horizontal eye saccades (REH), slow and fast smooth pursuit (SPS, SPF), optokinetic nystagmus (OKN) and horizontal gaze stabilization test (GST). Briefly, during all tests the examiner watched the participant's eyes for overshoot or disconjugate eye movement as well as the participant's ability to fixate on the appropriate target. SPS, SPF, and REH were used to test the participant's ability to follow a slow- or fast-moving target with their eyes. OKN was evaluated by having the participant view a moving striped visual stimulus on an iPad in the visual field in order to expose participants to a fast moving optic flow field to elicit nystagmus and potentially to induce S/S. Lastly, the GST was performed and the ability to stabilize vision was assessed while the participant fixated on a single point while rapidly rotating the head back and forth (as if indicating "no"). This test elicits the vestibular ocular reflex (VOR), compensatory eye movements driven by the vestibular system, which stabilizes the image on the fovea throughout head movement.

Signs of Oculomotor Dysfunction

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Near point of convergence (NPC) and King-Devick (KD) tests were also performed in order to assess each participant's oculomotor function. NPC was performed as previously described.[9,19] A convergence insufficiency is the inability to maintain binocular focus causing diplopia or accommodation difficulties resulting in blurriness. This may be a sign of diminished saccadic movement speed and/or cognitive and language processing.

Statistical Analysis

Group differences in demographics at initial assessment were analyzed using a one-way ANOVA. Group differences in KD, NPC, and symptom provocation following each clinical test at the three time points (baseline, 2 weeks and 6 weeks) were analyzed using a mixed-model repeated measures ANOVA. Data normality was examined by looking at the skewness and kurtosis followed by viewing scatter and box and whisker plots. In cases where the data were not found to be normally distributed non-parametric analysis using Kruskal-Wallis and Mann-Whitney tests for between-group comparisons were performed. Additionally Friedman's test and Wilcoxon's signed ranks test for repeated measures analysis were used, which are appropriate for ordinal scale measures. A logistic regression for binary outcomes ("Enter Method" and "Forward Conditional") was performed to examine the predictive validity of symptom provocation during vestibular and oculomotor assessments when combined with NPC and KD. Accuracy was calculated as the sum of the true positives and true negatives divided by the total sample size. All statistical analyses were conducted using SPSS software (version 22.0; IBM Corporation, Armonk, NY) and significance was set at alpha less than or equal to 0.05. Bonferroni correction was used to adjust p-values for multiple comparisons.

RESULTS

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Demographic data

Means and standard deviations between groups are reported in **Table 1**. There were no differences in sex, height, weight, or age. The healthy group was different from the acute concussion and delayed recovery group in both years' experience in primary sport (p=.006) and number of previous self-reported concussions (p<.001).

Change in outcome measures over time

The mixed-model repeated measures ANOVA revealed significant between-group differences across time in KD time ($F_{4,144}$=3.71, p=.007). KD time improved across time relative to baseline at both 2 weeks (p=0.04) and 6 weeks (p=.002) for the prolonged recovery group; however, the acute group did not significantly improve until the 6 week time point (p=.001). Although NPC demonstrated between group differences ($F_{2,70}$=8.53, p<.001) there was not a significant change across time ($F_{4,140}$=1.05, p=.38). The combined symptom provocation scores showed differential change over time for the acute and prolonged PCS groups ($F_{4,150}$=7.47, p=.007). The reduction in symptom provocation across time relative to baseline was present at both 2 weeks (p=.005) and 6 weeks (p=.005) for the acute group. Though, the prolonged PCS group did not significantly improve until the 6 week time point (p=.037). The changes across time for each individual outcome measure were as follows: GST symptoms showed no change across time; REH symptoms improved after 2 weeks in the acute group only (p=.003); SPS symptoms showed no change across time; SPF symptoms improved after 2 weeks (p=.024) and 6 weeks (p=.038) in the acute group, with no other changes across time observed; OKN symptoms improved after 2 weeks (p=.027) and 6 weeks (p=.041) in the prolonged recovery group, with no other changes across time observed. No significant differences were displayed in clinical measures between any of the time points and the healthy participants (Fig 1).

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Between group difference in concussion outcome measures

Follow the initial mixed models repeated measures ANOVA follow up Mann-Whitney tests were performed to further explore group differences for each of the clinical tests (see **Table 2).** Statistically significant differences in provoked symptoms between acutely concussed group and healthy participants at baseline were observed for the GST (p=<.001), REH (p=<.001), SPS (p=.004), SPF (p=<.001) and OKN (p=<.001) as well as the total combined number of symptoms provoked score (p=<.001). Additionally, mean NPC was higher in the acutely concussed group (5.4±2.8cm) compared to the healthy control group (3.4±1.9cm). A significant difference between the healthy participants and delayed recovery participants was also observed at baseline for NPC (p=.004) as well as symptoms provoked following the GST (p=.001), REH (p=<.001), SPS (p=.001), SPF (p=<.001), OKN(p=<.001) tests. At the 2 week time point the only significant difference between the healthy and acute concussion group was for symptoms following the OKN test (p=<.001), while significant differences between the healthy and delayed recovery group were only found between symptoms following SPS (p=<.001) and SPF(p=.001) tests.

Discriminating healthy from concussed participants

Mann-Whitney test revealed no significant difference between the acute concussion and the post-concussion groups. Therefore, these groups were combined and a logistic regression model for binary outcomes (healthy vs. concussed) was performed by testing the assessments, which were found to differ between baseline group statuses (**Table 2**). A multivariate logistic regression for binary outcomes using the “Enter” method was performed first (**Table 3**). This analysis identified the best subset of independent predictors of concussion as NPC, and number of symptoms following the REH, OKN, GST tests (accuracy=89.9%, p=.001). A second assessment using the “Forward conditional” method was performed in order to evaluate the

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effectiveness of summing S/S scores across all clinical tests and produced a second model with NPC plus GST and Combined S/S. This model could predict group status with 91% accuracy (p=<.001).

DISCUSSION

The results of the present study show a brief test battery that requires no specialized equipment or extensive training can accurately (91%) differentiate between healthy individuals and concussed athletes. Moreover, when performed at intervals following the initial evaluation, progress can be tracked and help in a return to play decision. Timely evaluations that are both sensitive and specific are crucial to making appropriate decisions whether to remove an athlete from competitive play or return them to the competition in the event of a suspected concussion. Many considerations such as the risk of potential further damage,[22,23] legal implications,[24] expectations of peers,[3] and the player's willingness to accurately report must be weighed with the potential negative effects of withholding an athletic that could have otherwise competed.[25] This decision must oftentimes be made on a sideline or in a casual sports setting where expensive assessment tools may not be readily available.

Symptoms: what are they and what do they mean

Current concussion position statements define a concussion as a pathomechanical event that elicits one or more symptoms.[7,21] Therefore, much is known about concussion signs and symptoms such as headache, dizziness, nausea, and fatigue.[26,27] However, these symptoms are not unique to concussion, and manifest as a results of numerous other pathologies such as whiplash,[4] exertional heat illness,[28,29] exertional sickling,[30] dehydration,[31] sleep deprivation or simply hunger. This high incidence of comorbidity between concussion S/S and overlapping pathologies has directed recent research to examine these symptoms further, and

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aims to identify specific damaged structures and processing pathways associated with each symptom.[6,8,32] Clinical tests such as NPC, KD, GST, SPS, SPF, and OKN have been well-suited to test the volitional and reflexive vestibular and oculomotor function.[19,33] Recent investigations of clinical testing following concussion have reported that perhaps as important as the presence and number of symptoms following a suspected concussion is whether or not these symptoms intensify during clinical testing or exercise.[4,9,20,34] The results from the present study demonstrated significant between-group differences in NPC and in symptoms provoked during the GST (<.001), REH(<.001), SPS(.004), SPF (<.001) and OKN(<.001) test, when comparing healthy controls and concussed participants at their initial test session independent of number of baseline symptoms. Moreover, these differences were also observed between healthy participants and those suffering from persistent symptoms (Table 2). Symptom provocation during a selected clinical test that assesses the vestibular and/or oculomotor pathway can potentially provide vital information about the location and severity of the potential injury. This information can aid in designing a management plan and return to play progression.

Differentiating the concussed from the healthy

The results of the current study suggest that a short screening, which requires minimal equipment can differentiate between healthy and concussed individuals with up to 91% accuracy. Our previous studies indicated that including symptom provocation using OKN test, NPC, KD and a SOT could differentiate concussed individuals from healthy controls with 98% accuracy.[9] The present study suggests that even without the SOT, which requires advanced postural analysis equipment, concussions can be detected with a high degree of accuracy. Other recent studies also report that including a brief vestibular/oculomotor exam increases the likelihood of diagnosing a concussion by 50%.[8] Increased accuracy allows those athletes who

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have suffered a concussion to receive the care they need and minimizes the risk of a false positive concussion diagnosis allowing healthy individuals to return to play.

A second primary goal of the present study was to track symptoms in both the acute and prolonged recovery groups relative to a healthy control group. It is significant to note that by the 2-week time point no significant differences remained between the acute group and healthy controls for any of the outcome measures. Suggesting, that two-weeks was a sufficient time for the acute group to return to a healthy state. However, comparing the prolonged recovery group to the healthy controls significant differences in NPC and symptom provocation following SPS and SPF and total symptom provocation score were evident at the 2-week and 6-week time points.

Some limitations should be noted. First, no baseline data were gathered for the acute concussion group or the prolonged recovery group and therefore all post injury evaluations had to be compared to healthy controls as opposed to their own baseline. Additionally, while we were able to collect data at all three time points for 51 of our healthy controls, only a total of 15 participants from the acute concussion group and seven from the delayed recovery group completed all three time points. The reduction in group size over the course of the three time points weakens our ability to generalize the results of our study. Future research on the progression of S/S at concurrent time points following an initial diagnosis is warranted to investigate the utility of these clinical tests in return to play management. Second, the use of subjective symptom reports was present in the current study, which may inherently affect reliability due to subjectivity, fidelity, and motivation. This point also contributes to a third limitation associated with any attempt to precisely categorize the various stages of concussion recovery. Across the concussion literature, differing definitions of acute, subacute, and post-concussion syndrome are used, which is in part due to the fact that diagnosis of concussion is

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based on symptomatology. It is commonly accepted that symptoms following concussion resolve with 7-10 days however,[7] identification of S/S are largely dependent on the sensitivity of the outcome measure used and the subjective accuracy of symptom self-report. Although our classification of prolonged recovery in this study was based on the currently accepted timeline of recovery, depending on what biomarkers for concussion may be identified in the future, classification categories of concussion may change and therefore must be viewed with caution. Despite these limitations, significant results and excellent accuracy were found using the current battery of tests.

CONCLUSIONS

These findings suggest that a brief ocular-motor screen including NPC, KD, GST, SPF, SPS and OKN can aid in the diagnostic process when evaluating for a suspected concussion. Moreover, repeating the same screening at regular intervals following an initial diagnosis of a concussion may aid in return to play protocol and track the healing process. The findings also reiterate the importance of symptom provocation following clinical testing suggesting that perhaps more important than baseline symptoms is change in symptom score following testing.

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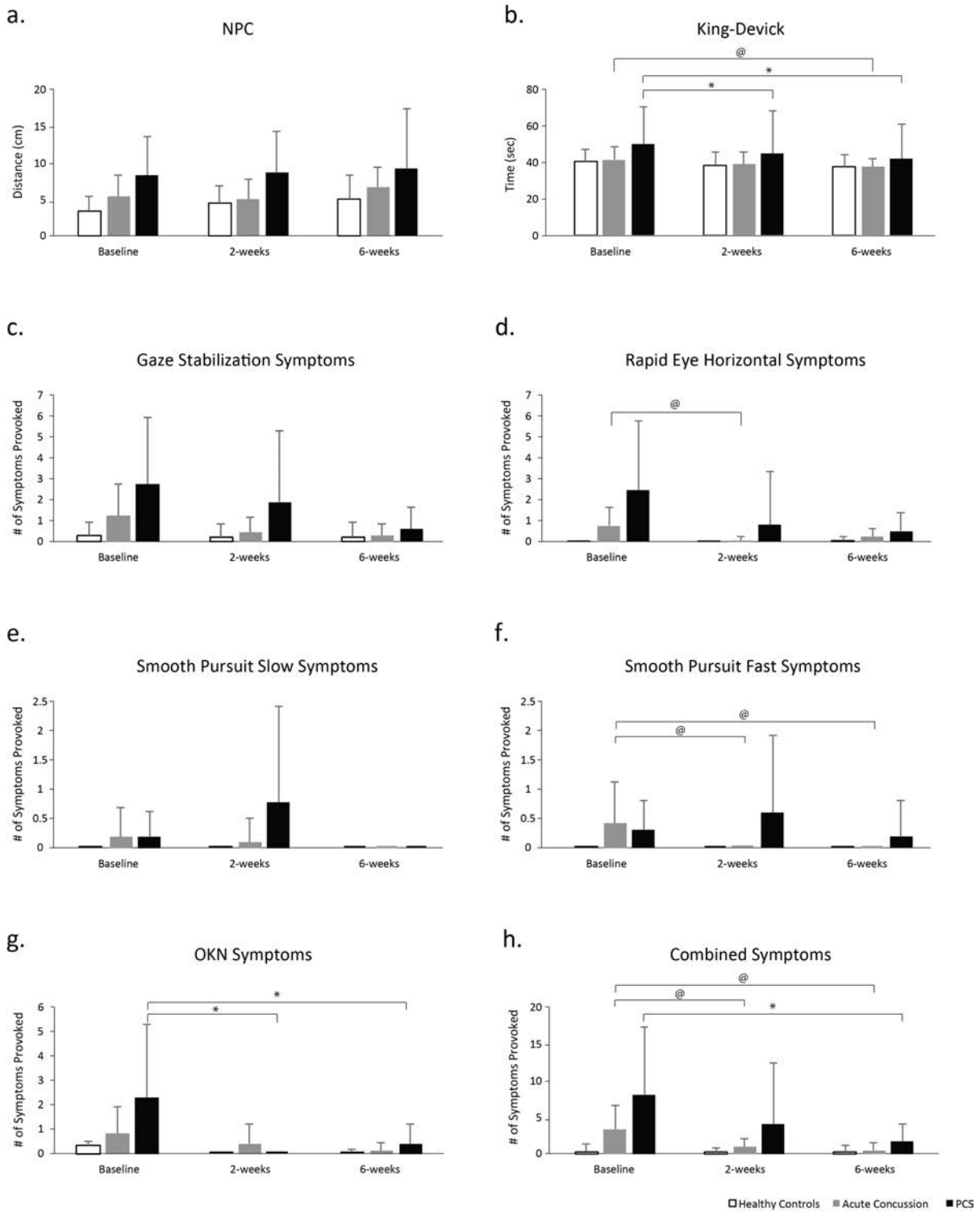
a.
NPC
Distance (cm)
20
15
10
5
0
Baseline
2-weeks
6-weeks
b.
King-Devick
@
*
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Time (sec)
80
60
40
20
0
Baseline
2-weeks
6-weeks
c.
Gaze Stabilization Symptoms
# of Symptoms Provoked
7
6
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1
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2-weeks
6-weeks
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Rapid Eye Horizontal Symptoms
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7
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5
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Baseline
2-weeks
6-weeks
e.
Smooth Pursuit Slow Symptoms
# of Symptoms Provoked
2.5
2
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Baseline
2-weeks
6-weeks
f.
Smooth Pursuit Fast Symptoms
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Baseline
2-weeks
6-weeks
Healthy Controls
Acute Concussion
PCS

Table 1: Descriptive characteristics of participants enrolled in study.

Variables	**Healthy N=58 M±SD**	**Acute Concussion N=21 M±SD**	**Prolonged Recovery N=10 M±SD**	**P**
Age	21.68±3.7	20.57±2.37	20.5±2.7	.289
Height	173.30±9.4	174.37±10.6	178.56±9.9	.336
Weight	71.17±12.2	75.68±15.85	75.06±8.1	.332
Years' Experience	10.55±5.4	6.11±6.2	6.88±3.1	.006*
Previous concussions	.34±.8	.95±1.1	4±3.3	.000*
Sex (%)				.436
Male	35(60%)	15(71.4%)	7(70%)	
Female	23(40%)	6(28.6%)	3(30%)	

M (Mean), SD (standard deviation), n (number). *significance at $p<0.05$

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Table 2. Means and standard deviations of concussion assessment scores across recovery time.

	Group			P-Value		
	Healthy M±SD	Acute M±SD	Prolonged Recovery M±SD	Healthy vs. Acute	Healthy vs. Prolonged Recovery	Acute vs. Prolonged Recovery
BASELINE						
	N=58	**N=21**	**N=10**			
NPC (cm)	3.41±1.9	5.37±2.8	8.19±5.3	.020*	.004*	.114
KD (sec)	40.1±6.6	41.1±7.3	49.6±20.4	.641	.096	.214
GST S/S Score	.25±.71	1.23±1.5	2.75±3.17	<.001*	<.001*	.201
REH S/S Score	0.0±0.0	.76±.83	2.45 ±3.3	<.001*	<.001*	.268
SPS S/S Score	0.0±0.0	.19±.51	.2±.42	.004*	.001*	.852
SPF S/S Score	0.0±0.0	.42±.7	.3±.5	<.001*	<.001*	.917
OKN S/S Score	.34±.18	.84±1.1	2.3±1.3	<.001*	<.001*	.164
Combined S/S	.36±.99	3.38±3.3	8.1±9.16	<.001*	<.001*	.173
2 WEEK						
	N=52	**N=20**	**N=10**			
NPC (cm)	4.46±2.	4.9±2.85	8.51±5.6	.756	.010*	.046
KD (sec)	4	38.6±6.7	44.3±23.6	.950	.954	.779
GST S/S Score	38.2±7.	.45±.7	1.9±3.4	.050	.004*	.194
REH S/S Score	1	.05±.2	.8±2.5	.107	.023*	.576
SPS S/S Score	.21±.6	.10±.4	.78±1.6	.107	<.001*	.141
SPF S/S Score	0.0±0.0	0.0±0.0	.6±1.3	1.00	<.001*	.042
OKN S/S Score	0.0±0.0	.41±.8	0.0±0.0	<.001*	1.00	.122
Combined S/S	0.0±0.0	.95±1.1	4.0±8.3	<.001*	.004*	.650
	0.0±0.0					
	.21±.6					
6 Weeks						
	N=51	**N=15**	**N=7**			
NPC (cm)	4.93±3.3	6.64±2.6	9.17±8.08	.059	.043	.739
KD (sec)	6	37.3±4.5	41.8±18.3	.773	.937	.698
GST S/S Score	37.0±6.4	.27±.6	.6±1.07	.457	.133	.481
REH S/S Score	.22±.67	.2±.4	.5±.84	.040	.005*	.435
SPS S/S Score	.04±.19	0.0±0.0	0.0±0.0	1.00	1.00	1.00
SPF S/S Score	0.0±0.0	0.0±0.0	.2±.6	1.00	.024*	.237
OKN S/S Score	0.0±0.0	.13±.4	.4±.84	.065	.015*	.543
Combined S/S	.02±.14	.53±1.1	1.7±2.4	.294	.004*	.243
	.27±.87					

NPC (Near Point of convergence). KD (King-Devick Test, total time), GST (Gaze stabilization test), REH (rapid eye horizontal), SPS (slow smooth pursuit), SPF (fast smooth pursuit), OKN (optokinetic reflex), Combined S/S (sum of symptoms provoked during each of the 5 clinical tests), S/S Score (difference between baseline symptoms severity score and symptom severity score following clinical test)*Significant between group difference at Bonferroni corrected p=.025

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Table 3. Concussion assessment model-binary logistic regression

Variables	**β**	**SE**	**Wald X^2**	**p**
Oculomotor score model (89.8%)				
NPC	.730	.253	8.303	.004*
REH s/s	3.27	1.554	4.437	.035*
OKN s/s	3.51	1.273	7.606	.006*
Constant	-5.391	2.94	3.35	.067
Convergence+Combined (91%)				
NPC	.742	.244	9.220	<.001*
GST s/s	-5.031	1.94	6.719	.010*
Combined s/s	3.735	1.166	10.27	<.001*
Constant	-5.742	1.458	15.506	<.001 *

SE (standard error), NPC (Near Point of convergence). GST (Gaze stabilization test), REH (rapid eye horizontal), OKN (optokinetic reflex), S/S (difference between baseline symptoms severity score and symptom severity score following clinical test). *Significance at $p<0.05$

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Appendix 10

Stress-Related Mental Health Symptoms and Neurocognitive Function in Active Duty Coast Guard Personnel

Richard J. Servatius, Justin D. Handy, Michael Doria, Catherine E. Myers, Christine E. Marx, Robert Lipsky, Corinna E. Lathan, Nora Ko, Pelin Avcu, W. Geoffrey Wright, & Jack W. Tsao

ABSTRACT

BACKGROUND: Little is known regarding stress-related mental health of active duty U.S. Coast Guard (USCG) personnel. Less is known concerning the interplay of stress-related mental health disorders, personality, and neurocognitive performance in USCG personnel. METHODS: 241 USCG personnel (22% female) participated. Participants completed a battery of scales including the posttraumatic stress disorder (PTSD) checklist (PCL) with military (PCLM) and nonmilitary (PCLNM) prompts to screen for probable PTSD (pPTSD), and Psychological Health Questionnaire (PHQ-8) for probable depressive disorder (pDD). Neurocognitive performance was assessed with the Defense Automated Neurobehavioral Assessment (DANA) battery. RESULTS: PCLM and PCLNM cluster scoring yielded pPTSD of 6% and 13%, respectively, with overall rate of pPTSD of 15%. pDD was 15% using aggregate scoring. In hierarchical logistic regression pPTSD was predicted by combat exposure, BI temperament and Type D personality. pDD was predicted by combat exposure, female sex, and Type D. pPTSD was associated with poorer recognition memory, whereas pDD was associated with deficits in Go/No-Go (GNG) throughput. In multinomial regression, Type D personality predicted pPTSD, pDD and comorbid pPTSD/pDD. BI temperament predicted comorbid pPTSD/pDD, whereas GNG throughput classified pDD. CONCLUSIONS: Stress-related mental health symptoms are apparent in USCG to the degree of larger military agencies and civilian first responders. Diathesis models linking individual vulnerabilities (BI temperament, Type D personality and sex) with traumatic experiences provide structure to the understanding of stress-related mental health issues in active duty military. A model including personality factors and objective neurocognitive tests identified and distinguished pPTSD from pDD.

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INTRODUCTION

As a military force, the United States Coast Guard (USCG) serves under the Department of Homeland Security, but under the Department of Defense (Navy) in times of war. The USCG has various missions: search and rescue, law enforcement, environmental protection, and maritime homeland security. Like the larger military branches, USCG personnel are at risk for emotional difficulties related to stress: posttraumatic stress disorder (PTSD) and major depressive disorder (DD). However, USCG personnel are a relatively understudied population with respect to PTSD and DD.

In its current formulation, PTSD is defined by the induction of symptoms in the aftermath of trauma among four categories: intrusive memories and recollections (Criteria B), avoidance of stimuli associated with the trauma (Criteria C), negative cognitions and mood (Criteria D), and enhanced arousal associated with the trauma (Criteria E). Occupational hazards of deployment and combat compound risk from base rates upon entry into service [1]. Among the larger military services, rates of probable PTSD (pPTSD) for active duty personnel acquired during large survey studies range from rates of about 5% prior to combat deployment to 15-20% after combat deployment [2-5]. Army service (regulars and Guard) is associated with the highest rates of pPTSD, followed by the Marines, Navy and Airforce [6]. These prevalence rates are echoed in hospitalizations for PTSD among the military with Army and Marines having the highest rates, with much lower rates among the Navy and Airforce; the Coast Guard had the lowest rates of hospitalizations for PTSD [7]. Given the relatively low level of help-seeking among military personnel [5], hospitalization codes are useful to compare branches of service, but likely severely underestimate incidence. With the first response and law enforcement aspects of Coast Guard service, rates of PTSD among their civilian counterparts are germane. Similar to the military,

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civilian rates of PTSD are sampled after singular common events or in the midst of normal ongoing operations. Sampling of first responders after common events finds rates ranging from 1-2% after the Norway attack of 2011[8], to 12% after the World Trade Center attack in 2001 [9], to 19% after Hurricane Katrina [10]. In cross sectional studies not involving a particular common event, rates of pPTSD among first responders vary from 4% [11; 12] to 18% [13].

Major depression or dysthymia is marked by various presentations of anhedonia, helplessness/hopelessness, difficulty concentrating, sleep disturbances, fatigue, changes in appetite, and suicidality. Like PTSD, DD occurs in active duty military and becomes manifest in association with extreme stressors such as combat [5; 14-19]. Rates for probable major depressive disorders (pDD) in active duty military generally mirror pPTSD in that rates of pDD are generally low pre-deployment and increase after deployment/combat [16; 17; 20; 21]. Rates of hospitalizations for DD among USCG personnel are about half that of Army, and similar to Air Force, Navy and Marines [7]. Similar to PTSD, rates of major depression derived from cross sectional studies in first responders vary from 3.5 % [12] to 16% [22] after unspecified critical incidents to 27% after Hurricane Katrina [23].

Trauma, more commonly experienced during stress of deployment and combat, is but one aspect underlying PTSD and DD in military personnel. Diathesis models link inherent vulnerabilities to traumatic experiences in refining risk for PTSD and DD during military service. There is a growing literature relating personality dispositions to PTSD and DD. For example, behaviorally inhibited (BI) temperament [24; 25] predicts biases of learning in civilians and veterans [26-29] and PTSD symptoms in veterans [26]. Distressed (Type D) personality is associated with worse medical outcomes [30] and is associated with DD [31; 32] and PTSD [33;

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34]. The extent that BI and/or Type D are associated with stress-related mental health difficulties in active duty US military is unknown.

Beyond the development and expression of mental health difficulties, there is growing concern that neurocognitive performance may degrade and adversely affect operational performance. In active duty military, neurocognitive deficits have been reported after mild traumatic brain injury (mTBI) [35; 36], repetitive military environmental exposures (e.g., blasts) [37], or accompanying, or as the result of, stress-related mental disorders [37-39]. The Defense Automated Neurobehavioral Assessment (DANA) battery, developed as a clinical decision support tool, consists of a battery of neurocognitive tests as well as psychological assessments [36; 40]. Lifetime TBI, especially multiple experiences, was found to affect simple reaction time upon second testing, with the model adjusting for pPTSD and pDD [36]. However, the impact of pPTSD and pDD were not separately evaluated.

A cross sectional study was conducted in active duty USCG personnel serving small boat stations. USCG service in small boat stations is similar to first response units with rotating shift schedules which mix on-duty and off-duty days on a weekly basis for many personnel. To gain insight into the source of traumatic stress symptoms, personnel were asked to complete posttraumatic stress disorder checklists (PCL) with a military (PCLM) and a nonmilitary (PCLNM) trauma in mind. Neurocognitive performance was assessed with the DANA. In addition, personnel were administered BI and Type D scales. We expected rates of pDD and pPTSD to be on the order of rates found in the larger military services. Further, we expected personality scales to provide unique or distinguishable contributions to stress-related mental health difficulties, with BI temperament predicting pPTSD whereas Type D personality would predict general distress. We further expected pDD and its psychomotor slowing to be reflected

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in deficits in reaction time tasks and attentional processing, whereas pPTSD would be associated with memory difficulties.

MATERIALS AND METHODS

Participants and Recruitment

Data were obtained as part of a larger study *Cognitive Assessment in Coast Guard Personnel: Neuroendocrine, Genetic and Epigenetic Correlates*, with collection during the period of 2014-2015. Recruitment was conducted by designated experimenters at eight small boat USCG Stations (Golden Gate, St. Petersburg, New York, San Francisco, Seattle, Port Canaveral, New Orleans, and Port Lauderdale). Active duty military participants (N = 241; 52 females and 189 males) were recruited during 'all hands;' 'all hands' was followed by individual consenting for those interested in participating. Designated ombudsmen ensured that potential participants understood that participation was voluntary and refusal to participate involved no penalty or loss of benefits within USCG. USCG personnel were not compensated for participation. Eligibility was contingent on not having a Deployment Limiting Medical Condition (DLMC) as defined in the Coast Guard Medical Manual, CODDTINST 6000.1 (Series). The study was reviewed and approved by the USCG Institutional Review Board.

Measures

Posttraumatic Stress Symptoms. To capture sources of trauma symptoms, two versions of the Posttraumatic Stress Disorder Checklist (PCL) were administered: one with a military stress prompt (PCLM) and one with a non-military prompt (PCLNM). Except for the prompts, the questions were identical. However, the PCLM was electronically administered on the DANA, whereas the PCLNM was on paper. The PCL assesses symptoms severity in the past month from 17 items; each item is scored on a 5 point Likert scale (0-5) yielding a range of 17-85.

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Specific questions correspond to DSM-IV symptom clusters including cluster B (re-experiencing the traumatic event), cluster C (avoidance/numbing), and cluster D (increased arousal). The PCL has convergent reliability and validity with sensitivity and selectivity for the diagnosis of PTSD (using DSM IV criteria). The PCLs were scored by two methods: 1) a total score of >50 and 2) cluster scoring corresponding to the requirements of PTSD diagnosis which require a score of 3 or greater on: one Cluster B symptom, three Cluster C symptoms and two Cluster D symptoms [41-44].

Depressive Symptoms. The Patient Health Questionnaire -8 (PHQ-8) was used to assessed how often depressive symptoms were bothersome over the last two week period. Occurrence was rated 'not at all', 'several days', more than half the days', and 'nearly every day'. Two criteria for pDD were used: 1) total >9 [45], and 2) 5 of 8 questions rated at least 'more than half the days' with one of the symptoms either depressed mood or anhedonia [46].

Concussion History. The DVBIC TBI Screening Tool [47; 48] was used to assess present/lifetime mTBI status. Verbally and individually administered with each participant, the screening tool determines whether the participant experienced a head injury, whether the participant lost consciousness and for how long, and the degree current symptoms are attributable to head injury.

Type D. Distressed, or Type D personality, is composed of two constructs: negative affect (NA) and social inhibition (SI). A 14-item scale (DS-14) probes NA and SI with 7 questions each on a Likert scale. Those scoring 10 or above on both subscales are considered Type D [49].

BI Temperament. The Adult Measure of Behavioural Inhibition (AMBI) consists of 16 items probing aspects of BI temperament. Items assess the degree behaviors are exhibited in social and nonsocial situations on a three-point Likert scale (ranging from 'No/hardly ever' to 'Yes/most of

the time'). Total scores range from 0 to 32. Those with scores above 15.5 were classified as BI.

Combat Exposure. Combat was assessed with the Combat Exposure Scale (CES). At times of war, USCG personnel volunteering for combat duty serve in US Navy. The CES is a 7-item self-report survey of combat experiences assessing types of experiences, number of times experienced and number of involvements. Respondents were classified as either having previous combat exposure or not.

Neurocognitive tests. The DANA is a portable ruggedized computer device loaded with a battery of neurocognitive tests and psychological scales. The 'standard' version includes assessments of: simple reaction time (SRT), Code Substitution Learning (CS-L), procedural reaction time (PRT), Spatial Discrimination (SPD), Choice Reaction (Go/No Go; GNG), Code Substitution Recall (CS-R), Matching to Sample (MTS), Sternberg Memory Search (SMS), and a second SRT (SRT2). These tasks are followed by psychological scales: PCLM and PHQ-8.

The DANA has three versions: 'standard', 'rapid' and 'brief', which are distinguished by the extent of the tests and batteries administered. For the first 31 participants the 'rapid' was administered, for all others 'standard'. For these 31 participants, PHQ-8 data is missing; PCLM was administered in paper form. Also for these 31 participants, neurocognitive testing was restricted to SRT, PRT and GNG.

Analytic Approach. Scales were assessed for reliability and inter-relatedness, which is depicted in Table 2. For mental health outcomes, hierarchical logistic regression was used. In model building, we included stable preexisting personal characteristics (Sex, BI, and Type D) and preexisting experiential characteristics (History of Concussion) in Model 1, with experiential characteristics of military service (Deployment, and Combat Exposure) entered into Model 2. This model was extended to the assessment of neurocognitive performance using hierarchical

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linear regression, with mental health outcomes (pPTSD and pDD) included as predictors in a third model. Multinomial logistic regression was used to identify factors significantly related to pPTSD, pDD, and co-occurring pPTSD/pDD; those factors which failed to reach significance in earlier models were dropped from multinomial regression.

RESULTS

Demographic Features of the Sample. Recruitment within small boat stations yielded a diverse group of participants. Demographic characteristics of the study sample are presented in Table 1. A range of ranks volunteered, from newly enlisted and junior grade to officers (highest rank at small boat stations). The overall percentage of females in USCG is ~15%; our sample contained 22% females. Categorical factors are divided by Sex with χ^2 analyses of distributions. Whereas the sample was generally young (65% younger than 30 years old), females were disproportionately younger with 91% younger than 30. Females in the sample were also disproportionately lower in rank. Lifetime history of concussion differed with higher proportion of males experiencing a concussion than females.

Table 1.Demographic Characteristics of the USCG Sample

	Overall	**Male**	**Female**
Age	***N* = 241**	***N* = 189**	***N* = 52**
<25 years	74 (31%)	43 (23%)	31 (60%)
25-29 years	82 (34%)	66 (35%)	16 (31%)
>29 years	85 (35%)	80 (42%)	5 (9%)
Ethnicity	***N* = 241**	***N* = 189**	***N* = 52**
White/Non-Hispanic	176 (73%)	140 (74%)	36 (69%)
Black/Non-Hispanic	8 (3%)	7 (4%)	1 (2%)
Hispanic	35 (15%)	25 (13%)	10 (19%)
Other	22 (9%)	17 (9%)	5 (10%)
Education	***N* = 241**	***N* = 189**	***N* = 52**
Some college or less	197 (82%)	157 (83%)	40 (77%)
Bachelor's or higher	44 (18%)	32 (17%)	12 (23%)

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Lifetime History of Concussion	***N* = 241**	***N* = 189**	***N* = 52**
Yes	117 (49%)	105 (56%)	12 (23%)
Rank	***N* = 236**	***N* = 185**	***N* = 51**
Cadet	7 (3%)	3 (2%)	4 (8%)
Junior Enlisted (E1-E4)	119 (50%)	78 (42%)	41 (80%)
NCO (E5-E6)	91 (39%)	86 (46%)	5 (10%)
Senior NCO (E7-E9)	12 (5%)	12 (6%)	0
Officer	7 (3%)	6 (3%)	1 (2%)
Deployment	***N* = 233**	***N* = 184**	***N* = 49**
Previously Deployed	104 (45%)	94 (51%)	10 (20%)
Combat Exposure	***N* = 232**	***N* = 181**	***N* = 51**
Yes	20 (9%)	19 (11%)	1 (2%)
Type D	***N* = 240**	***N* = 188**	***N* = 52**
Type D	76 (31%)	58 (31%)	18 (35%)
BI	***N* = 241**	***N* = 189**	***N* = 52**
Inhibited	89 (37%)	70 (37%)	19 (37%)

Psychometric Properties of the Scales. The reliability and intercorrelations of the PCLs, PHQ-8, DS-14, and AMBI are presented in Table 2. As expected, the PCLs were highly correlated with PHQ-8, with personality scales highly related to PCLs and PHQ-8. Cronbach's α was in the acceptable range for all measures.

Table 2.Relaibility and Interrelatedness of Scales

	1	2	3	4	5
1 PCL-M	-				
2 PCL-C	.69**	-			
3 PHQ-8	.70**	.64**	-		
4 DS14	.49**	.56**	.61**	-	
5 AMBI	.37**	.43**	.33**	.51**	-
Mean	25.71	28.95	4.80	19.53	14.17
St.Dev	9.83	11.65	4.67	8.62	5.69
Range	17-69	17-66	0-20	3-46	3-30
Chronbach's α	.92	.93	.87	.89	.83

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Caseness for PTSD and Depression. Caseness was determined by aggregate and symptom scoring for both pPTSD and pDD (See Table 3). The differences in stringency did not affect caseness with respect to sex. Inasmuch as the two more liberal criteria for PTSD and DD, symptom and aggregate scoring, respectively, have acceptable rates of sensitivity and selectivity, these criteria were used for pPTSD and pDD for all subsequent analyses.

Table 3. Comparison of PCLM and PCLNM Responses in USCG Sample

	None *N* = 204	**Probable PTSD PCL-M** *N* = 5	**Probable PTSD PCL-NM** *N* = 22	**Probable PTSD PCL-M and PCL-NM** *N* = 10
PCL-M				
Total Score	22.99 (5.55)	53.60 (12.93)	32.18 (7.93)	53.20 (10.81)
Cluster B	0.19 (0.60)	3.40 (1.82)	0.45 (1.10)	2.80 (1.32)
Cluster C	0.30 (0.74)	4.60 (1.82)	1.00 (1.20)	5.10 (1.66)
Cluster D	0.71 (1.06)	4.00 (1.00)	2.45 (1.26)	4.00 (1.25)
PCL-NM				
Total Score	25.27 (7.22)	32.00 (3.16)	48.27 (7.47)	59.80 (5.47)
Cluster B	0.55 (1.02)	1.20 (1.30)	3.14 (1.32)	3.70 (0.95)
Cluster C	0.58 (1.02)	1.20 (1.30)	4.09 (1.19)	6.00 (1.05)
Cluster D	0.86 (1.21)	2.20 (1.92)	3.05 (1.00)	4.30 (0.68)

Comparison of PCLM and PCLNM. Providing two PCLs with different prompts – military and nonmilitary – allowed for a comparison of answers to each. The PCLs were separately evaluated; therefore, one could meet criteria using symptom scoring for pPTSD with either PCL or both. As seen in Table 4, participants distinguished symptoms as being associated with a military or nonmilitary trauma, with some expressing both. The number of USCG meeting criteria for PTSD using symptom clusters of PCLM was 15/241 (6%), and for PCLNM was 32/241 (13%), for an overall screening rate of 15%. Although it is expected that symptom scores

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of those meeting criteria are greater than those not meeting criteria, two comparisons related to caseness were of interest: 1) how distinct total scores were among those meeting caseness, and 2) the degree PCL scores of those meeting criteria on one of the scales differed from those meeting criteria on both. A 3 x 2 (Case Group x PCL) multiple analysis of variance (MANOVA) with post hoc Bonferroni corrected t-tests indicated that PCLNM total scores of those meeting criteria on both PCLs were greater than the PCLNM scores of those meeting criteria solely on the PCLNM scale (p <.05).

Table 4.Caseness of pPTSD and pDD in USCG Sample Sorted by Sex

	Total	Male	Female	
PCLM				
Aggregate	9/241 (3.7%)	8/189 (4.2%)	1/52 (1.9%)	$\chi^2(1) = 0.61$, $p = .437$
Symptom	15/241 (6.2%)	11/189 (5.8%)	4/52 (7.7%)	$\chi^2(1) = 0.25$, $p = .621$
PCLNM				
Aggregate	18/241 (7.5%)	15/189 (7.9%)	3/52 (5.7%)	$\chi^2(1) = 0.28$, $p = .599$
Symptom	32/241 (13.3%)	26/189 (13.8%)	6/52 (11.5%)	$\chi^2(1) = 0.17$, $p = .676$
PHQ-8				
Aggregate	31/210 (14.8%)	21/163 (12.9%)	10/47 (21.3%)	$\chi^2(1) = 2.04$, $p = .153$
Symptom	14/210 (6.7%)	11/163 (6.7%)	3/47 (6.4%)	$\chi^2(1) = .01$, $p = .929$

The age of self-referenced trauma for PCLNM provides insight into USCG experience and risk. Of those meeting criteria using PCLNM, 26% identified a trauma before the age of 18; of those not meeting criteria, 28% identified a trauma before age 18.

Neurocognitive Performance. Hierarchical linear regression examined factors predicting performance using three models: Model 1 (Type D, BI, and Concussion History), Model 2 (Deployment and Combat Exposure) and Model 3 (pPTSD and pDD). Table 5 presents the models when: 1) a significant model is indicated for at least one of the primary dependent measures, and 2) the significant model indicated significance in a major factor of interest (pPTSD, pDD, Deployment History, Combat Exposure). For SRT1 and SRT2, throughput was

the primary dependent measure. The models of SRT1 were not significant. For SRT2, pDD predicted worse performance. For CS-L and CS-R, percent correct and throughput were evaluated. For CS-L, percent correct was negatively impacted by Deployment History, whereas the model for throughput was nonsignificant. For CS-R, the models were not significant. For

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Table 5. Summary of Hierarchical Regression Analyses for Variables Predicting Neurocognitive Performance (Percent Correct and Throughput) in USCG Personnel (*N* = 241).

	Go/No-Go						Memory Search						Simple RT (Time 2)		
Variable	**% Correct**			**Throughput**			**% Correct**			**Throughput**			**Throughput**		
	B	***SE B***	**β**	***B***	***SE B***	**β**	***B***	***SE B***	**β**	***B***	***SE B***	**β**	***B***	***SE B***	**β**
Model 1															
Type D	0.01	0.02	.01	-4.59	2.79	-.12	-0.01	0.03	-.03	1.20	2.89	.03	-7.24	4.35	-.12
BI	-0.01	0.02	-.01	-5.47	2.70	-.15*	-0.03	0.03	-.08	-4.91	2.89	-.13†	-5.73	4.21	-.10
Lifetime History of Concussion	0.01	0.02	.02	-0.44	2.54	-.01	-0.01	0.03	-.02	-1.26	2.61	-.03	0.26	3.94	.01
R^2		.01			.05			.01			.02			.03	
***F* for change in R^2**		.04			3.14*			0.56			1.11			2.13†	
Model 2															
Type D	0.01	0.02	.01	-4.47	2.78	-.12	-0.01	0.03	-.03	1.21	2.90	.03	-7.08	4.34	-.12
BI	0.01	0.02	.02	-4.62	2.75	-.12†	-0.04	0.03	-.10	-4.75	2.85	-.13†	-5.72	4.28	-.10
Lifetime History of Concussion	0.01	0.02	.05	0.25	2.57	.01	-0.01	0.03	-.03	-1.08	2.66	-.03	0.37	3.98	.01
Deployment	-0.04	.02	-.18*	-3.74	2.69	-.10	0.04	0.03	.09	-0.70	2.76	-.02	1.19	4.15	.02
Combat Exposure	0.02	0.03	.05	-3.26	4.50	-.05	-0.04	0.05	-.06	-1.80	4.78	-.03	-11.66	7.02	-.12†
R^2		.03			.06			.02			.02			.05	
***F* for change in R^2**		3.01*			1.49			0.95			0.13			1.38	
Model 3															
Type D	0.01	0.02	.02	-2.21	2.85	-.06	0.01	0.03	.02	1.93	2.99	.05	-4.36	4.47	-.07
BI	0.01	0.02	.02	-3.63	2.76	-.10	-0.02	0.03	-.06	-3.79	2.89	-.10	-4.62	4.32	-.08
Lifetime History of Concussion	0.01	0.02	.05	0.52	2.52	.01	-0.01	0.03	-.03	-1.27	2.65	-.03	0.56	3.95	.01
Deployment	-0.04	0.02	-.17*	-2.96	2.65	-.08	0.04	0.03	.11	-0.59	2.77	-.02	2.32	4.14	.04
Combat Exposure	0.03	0.03	.06	-0.32	4.54	-.01	-0.02	0.05	-.02	-0.82	4.86	-.01	-8.17	7.13	-.08
pDD	-0.04	0.03	-.11	-10.60	3.88	-.21**	-0.03	0.04	-.05	2.30	4.01	.04	13.11	5.98	-.17*
pPTSD	0.02	0.02	.07	-2.46	3.68	-.05	-0.08	0.04	-.16*	-7.44	3.87	-.15†	-2.85	5.78	-.04
R^2		.04			.10			.04			.04			.07	
***F* for change in R^2**		1.15			4.56*			2.69†			1.86			2.87†	

Note: pPTSD, probable PTSD; pDD, probable depressive disorder; *B*, unstandardized coefficient, *SE*, standard error, β, standardized coefficient.
Significance levels associated with beta coefficient values and *F* for change in R^2: † $p < .10$, * $p < .05$, ** $p < .01$

PRT, percent correct responding was at ceiling, so throughput was the primary dependent measure. However, the model was not significant. The models for SPD, characterized by percent correct and throughput, were nonsignificant. For GNG, percent correct and throughput are primary measures. Those with Deployment History made slightly more errors (3%). pDD predicted worse performance in terms of throughput. The models for MTS, characterized by percent correct and throughput, were nonsignificant. For SMS, percent correct and throughput were evaluated. Those meeting screening criteria for pPTSD exhibited significantly more errors and marginally worse throughput.

Thus, those meeting screening criteria for pDD exhibited slower information processing in terms of SRT2 and GNG performance; whereas those meeting screening criteria pPTSD exhibited poorer memory performance.

Predictors of Mental Health Symptoms. As can be seen in Table 6**,** caseness of pPTSD was classified by BI, Type D and combat exposure, with roughly equivalent odds ratios. Caseness for pDD was classified by sex, Type D and combat exposure. Type D personality and combat experience increase the likelihood of developing stress-related mental health difficulties. BI temperament is more specific to pPTSD. The classifier strategy was extended to pPTSD, pDD and co-occurring pPTSD/pDD (See Table 7). Based on analyses of neurocognitive performance, GNG throughput was added to the model as a predictor. Again, Type D personality strongly classified all three groups. BI temperament and combat exposure classified co-occurring caseness of pPTSD/pDD. In contrast, GNG throughput classified pDD. A combination of psychological scales and neurocognitive tests support the contention that PTSD and depression in military personnel have distinct features.

Table 6. Predictors of Stress-Related Health Disorders in USCG Personnel Identified in Hierarchical Logistic Regression (N= 241).

	pPTSD *N* = 37			pDD *N* = 31		
Variable	***B (SE)***	**OR**	**95% CI**	***B (SE)***	**OR**	**95% CI**
Model 1						
Sex						
Male (ref)						
Female	-0.56 (0.54)	0.57	(0.20, 1.64)	0.86 (0.50)	2.36†	(0.88, 6.35)
Type D						
Non-Type D (ref)						
Type D	1.26 (0.41)	3.53**	(1.57, 7.92)	1.32 (0.44)	3.76**	(1.60, 8.83)
BI						
Non-Inhibited (ref)						
Inhibited	1.32 (0.42)	3.74**	(1.66, 8.43)	0.64 (0.44)	1.90	(0.81, 4.45)
Lifetime History of Concussion						
Negative (ref)						
Positive	-0.36 (0.42)	0.70	(0.31, 1.59)	0.56 (0.45)	1.74	(0.72, 4.21)
R^2_{CS}		.12			.09	
Model χ^2		$\chi^2(4) = 28.25$, $p = .002$			$\chi^2(4) = 18.76$, $p = .001$	
Model 2						
Sex						
Male (ref)						
Female	-0.36 (0.55)	0.70	(0.24, 2.07)	1.33 (0.56)	3.79*	(1.26, 11.43)
Type D						
Non-Type D (ref)						
Type D	1.27 (0.42)	3.55**	(1.56, 8.10)	1.35 (0.45)	3.85**	(1.58, 9.37)
BI						
Non-Inhibited (ref)						
Inhibited	1.29 (0.42)	3.62**	(1.58, 8.30)	0.53 (0.45)	1.70	(0.70, 4.15)
Lifetime History of Concussion						
Negative (ref)						
Positive	-0.39 (0.43)	0.68	(0.29, 1.58)	0.56 (0.48)	1.75	(0.68, 4.52)
Deployment						
Non-Deployed (ref)						
Deployed	0.29 (0.43)	1.34	(0.58, 3.09)	0.88 (0.47)	2.42†	(0.96, 6.11)
Combat Exposure						
No Exposure (ref)						
Combat Exposure	1.30 (0.61)	3.67*	(1.10, 12.21)	1.59 (0.60)	4.91**	(1.51, 15.96)
R^2_{CS}		.14			.14	
Model χ^2		$\chi^2(6) = 33.66$, $p < .001$			$\chi^2(6) = 30.79$, $p < .001$	

Note: pPTSD, probable PTSD; pDD, probable depressive disorder; *B*, logistic coefficient; *SE*, standard error; OR, odds ratio; CI, confidence interval; R^2_{CS}, Cox and Snell R^2; ref, reference category.
Significance levels: † $p < 10$, * $p < .05$, ** $p < .01$

DISCUSSION

Coast Guard personnel serving small boat stations experience shift duty with a mixture of operational stressors and compounding civilian stressors. To capture stress-related mental health

difficulties, USCG personnel were administered both the PCLM and PCLNM. Overall caseness of pPTSD was 15.4%, with caseness related to nonmilitary stressors at greater rates than military related stressors. Rates of military-related pPTSD were consistent with military and civilian first responders in cross sectional studies. Further, rates of caseness for nonmilitary-related pPTSD were similar to that of other military branches and civilian first responders. Rates of pDD also resembled other military branches and civilian first responders.

The USCG is increasing the number of females in active duty; the present sample contained 22% females participating. Rates of pPTSD were equivalent in male and female USCG personnel regardless of screening criteria of type of trauma experienced. Rates of pDD were equivalent in females, but female sex was a significant predictor of pDD.

There has been growing concern that mTBI may have long term mental and cognitive health consequences. Although roughly half the sample screened positive for lifetime mTBI, lifetime mTBI was not a predictor of pPTSD, pDD or any deficits neurocognitive performance.

However, neurocognitive performance was affected by mental health outcomes. pPTSD was associated with poor recognition memory, consistent with the work of others [50; 51]. pDD was associated with slower reaction times during the second administration of simple reaction time testing, and with slower reaction times during Go/No-Go testing. Sensitivity to neurocognitive deficits in PTSD and DD may depend on a number of factors: form and venue of testing, and population size.

The distinctiveness of PTSD and DD in military populations is in question with screenings typically finding a high degree of overlap in meeting criteria for both disorders. Type D personality was generally associated with pPTSD and pDD. However, BI temperament distinguished between pPTSD and pDD, with BI temperament strongly associated with pPTSD

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and as a classifier of co-occurring caseness of pPTSD/pDD. GNG throughput classified pDD, but not pPTSD or co-occurring pPTSD and pDD. A combination of personality and neurocognitive tests supports the contention that co-occurring PTSD and DD is more PTSD-like than DD-like. Assessment of personality dimensions may allow for early identification of at-risk individuals for assignment, intervention and treatment.

The main strength of the study is the examination of otherwise healthy high functioning active duty USCG personnel, an underrepresented military population. Not one participant was on reduced or modified duty. Another strength was the number of female volunteers, which allowed for assessments of the influence of sex in many of the outcomes. However, there are several weaknesses that need to be considered. For one, the sample was neither representative of all USCG small boats stations or of the general USCG force. For another, the cross sectional nature of assessment precludes sensitivity to fluctuations in emotional and cognitive performance. Although personality tendencies are assumed to be stable individual characteristics, the nature of the study does not preclude the possibility that experiences such as head injury or those leading to stress-related mental health symptoms concomitantly changed personality characteristics. Further, as a convenience sample of USCG at small boat stations, many of the cofactors considered (e.g., sex, deployment, CES) were unbalanced and resulted in small numbers when trying to identify interactions. For example, females in the sample were generally younger and concentrated in lower ranks than males. Small boat stations are heterogenous in military roles (boat crews, engineers, cooks, administrative and support staff) and shifts. The inclusiveness of the study to all willing participants comes at the expense of focus on particular roles, which would require a much larger study to capture. Additionally, testing was conducted on an individualized basis, therefore time of testing - within a range of

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0700 to 1700 – was not controlled. Volunteers were allowed to schedule testing when testing would not interfere with duty. Therefore, control was also not exerted in terms of type of experiences immediately preceding testing (e.g., operations, exercise, meals or training).

To date, this is the largest empirical study of stress and stress-related mental disorders in USCG personnel. The rates of pPTSD related to PCLM and PCLNM are provocative, generating questions for future studies. For example, the higher rates attributable to PCLNM with respect to PCLM are likely not attributable to early life experiences, *per se*. The self-identified ages of trauma for the PCLNM are similar between those meeting criteria and those not, with the experience of early trauma not predictive of meeting PCLM criteria. Further, two thirds of the self-identified traumas were experienced during the span of most military careers. The degree nonmilitary trauma is experienced in the larger military branches would be interesting to compare.

Personality factors in combination with GNG throughput classified those identified as pPTSD, pDD and both, with sensitivity and selectivity. Accounting for personality could provide opportunities for early intervention or targeted tracking to reduce expression of PTSD and/or DD in the aftermath of trauma. A combination of personality scales and cognitive testing could provide clinicians additional input for differential diagnoses of stress-relation mental health difficulties.

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Appendix 11

Facilitated Eyeblink Conditioning and Heightened Posttraumatic Symptoms in Active Duty Military Expressing Social Inhibition

Justin D. Handy, Pelin Avcu, Nora Ko, Alejandro Ortiz, Michael J. Doria, Richard J. Servatius

Abstract

OBJECTIVE: A learning diathesis model for posttraumatic stress disorder (PTSD) posits inherent positive biases in associative learning potentiate avoidance in the aftermath of trauma. Recently, we reported strong associations between behavioral inhibited (BI) temperament (withdrawal in the face of social and nonsocial challenges) and distressed (Type D) personality (negative affect combined with social inhibition) with probable PTSD in active duty Coast Guard (CG) personnel. We determined whether positive learning biases are apparent in BI and Type D as assessed through eyeblink conditioning using a partial reinforcement schedule. METHOD: 79 active duty CG personnel (15 females) were recruited from 5 Boat Stations. Participants were administered the PTSD checklist (PCL) with military (PCLM) and non-military (PCL-C) prompts (DSM-IV criteria). Eyeblink conditioning was accomplished with a 500-ms pure tone conditioned stimulus (CS) co-terminating with a 100-ms air-puff unconditional stimulus (US), with interpolation of 50% CS-alone trials. RESULTS: Consistent with earlier work, facilitated acquisition of the eyeblink response was apparent in BI temperament. Facilitation was also apparent in Type D personality, predominately related to the social inhibition component. Both personality dimensions were associated with greater PTSD symptoms. Rates of learning did not independently predict PTSD symptoms. CONCLUSIONS: Those expressing social inhibition and behavioral withdrawal displayed positive learning biases and stronger PTSD symptoms. Negative affectivity was associated with PTSD, but did not contribute to positive biases. These data in active duty military further support personality dimensions of inhibition and withdrawal as vulnerabilities to the development and expression of PTSD.

Facilitated Eyeblink Conditioning in Active Duty Military Expressing Type D Personality and BI Temperament

Although the experience of stressors consistent with trauma is fairly common, development of posttraumatic stress disorder (PTSD) is relatively rare [1, 2]. Diathesis models link vulnerabilities with risk in the development and expression of PTSD [3-8]. A learning diathesis model posits that symptoms of fear, horror, or dread and attendant memories are common, but the degree that symptoms persist and induce avoidance reflect inherent learning biases [9-11].

A means for assessing learning biases, independent of fear or dread, is through classical conditioning of the eyeblink response, an assessment of new motor learning. In eyeblink conditioning, a conditioned stimulus (CS) is paired with a reflex-inducing unconditional stimulus (US). Through successive pairings of the CS and US, an anticipatory eyeblink is elicited as a conditioned response (CR) to the CS. This new motor learning is dependent on the cerebellum [12] and influenced by the amygdala, hippocampus, prefrontal cortex, and nigrostrial pathway [13].

Positively biased learning, as assessed by eyeblink conditioning, is apparent in those with trait anxiety [14]. A component of trait anxiousness is behavioral inhibition (BI); that is, extreme withdrawal in the face of social and nonsocial challenges [15-17]. Similar to trait anxiety, positively biased learning is apparent and quite robust in BI temperament, having been observed in civilian adolescents [18] and adult samples [19-23], as well as under a variety of schedules and procedures. BI temperament is a vulnerability factor for anxiety disorders [24-28] and associated with PTSD [28-30]. Facilitated acquisition is also apparent in veterans with and without current self-reported posttraumatic symptoms, but expressing BI [28]. Enhanced eyeblink conditioning in BI may reflect greater intrinsic cerebellar connectivity [31-33].

Akin to BI, distressed (Type D) personality is marked by the tendency to experience negative affect (NA) coupled with high levels of social inhibition (SI). Although Type D personality was initially used to explain individual differences in morbidity and mortality associated with coronary heart disease [34], Type D predicts PTSD among survivors of myocardial infarction [35], as well as in non-patient groups, such as first responders [36] and active duty military personnel [37, 38]. Theoretical similarities between BI and the SI subcomponent of Type D (i.e., shared propensities for inhibitory behavior) suggest that individuals with distressed personality may also express facilitated eyeblink conditioning. This hypothesis is supported by longitudinal work pointing to a genetic basis for self-reported SI in adults, which has led to speculation that SI in adulthood may very well be preceded by BI in childhood [39]. Moreover, Kupper and Denollet [40] report strong concordance between Type D personality in adults and the expression of social anxiety disorder, which appears to be driven by the SI subcomponent of Type D in these individuals; social anxiety disorder is often preceded by BI during childhood [41, 42]. What remains unclear is the role the co-occurrence of high NA in Type D plays in associative learning. This is an important consideration, given the strong positive relationship between NA and depression [43, 44], and prior work reporting impairments in eyeblink conditioning associated with depression [45].

The objectives of the current study were twofold. Of primary interest was how associative learning was expressed in military personnel using eyeblink conditioning. This work complements previous studies reporting facilitated eyeblink conditioning in BI within civilian [21] and veteran samples [28], and further tested predictions of the learning diathesis model of stress and anxiety in an active duty military sample. Previous work has shown that partial reinforcement schedules, which include 50% paired trials and 50% CS-alone trials, are effective

in maximizing learning differences in those with BI temperament [19, 21]. This learning schedule was therefore employed in the current study.

A secondary focus was to assess the extent learning performance in eyeblink conditioning could independently classify personnel and predict mental health symptoms. Type D and BI were recently identified as significant predictors of probable PTSD in a larger study of CG personnel [46]. In the current study, a subset of this larger active duty sample was included which allowed for the exploration of the sensitivity and selectivity of the conditioned eyeblink response as a classifier of mental health complaints.

Materials and Methods

Participants

Data were collected as part of a larger cross-sectional study in cooperation with the United States Coast Guard, with data collection occurring during the period of 2013-2015. A total of 78 active duty CG personnel (64 males and 14 females) completed the study. CG personnel were recruited by designated experimenters from five CG Boat Stations: Station Golden Gate (Sausalito, CA; *N*= 23), Station St. Petersburg (St. Petersburg, FL; *N*=20), Station San Francisco (San Francisco, CA; *N*=11), Station Seattle (Seattle, WA; *N*=13), and Station Port Canaveral (Port Canaveral, FL; *N*=11). Active duty military participants were recruited at the beginning of the Stations' off going and on coming duty section period, followed by individual consenting for those interested in participating. Designated ombudsmen ensured that potential participants understood that participation was voluntary and refusal to participate involved no penalty or loss of benefits within CG. CG personnel were not compensated for participation. Eligibility was contingent on not having a Deployment Limiting Medical Condition (DLMC) as defined in the

Coast Guard Medical Manual, COMDTINST M6000.1F. The study was reviewed and approved by the CG Institutional Review Board.

Self-Report Measures

The Type D Scale (DS-14) [47] is a 14-item scale used to evaluate negative affectivity (NA) and social inhibition (SI). Both subscales contain seven items answered using a 5-point Likert scale, ranging from 0 (false) to 4 (true). Participants were classified as Type D if they scored 10 or greater on both NA and SI subscales. These cut-offs have demonstrated the greatest reliability in classifying individuals as Type D across general and clinical populations [48].

The AMBI is a 16-item self-report inventory that assesses current tendency to respond to new stimuli with inhibition and/or avoidance, and has also been shown to be a measure of anxiety proneness. "Uninhibited" individuals are defined as those scoring 2-15, whereas "inhibited" individuals score 16-32 [49].

The PCL-M and PCL-C were 17-item questionnaires used for inquiring about the presence and frequency of posttraumatic symptoms stemming from stressful military (i.e., PCL-M) and non-military (i.e., PLC-C) experiences. Participants rated symptom severity over the past month on a 4-point Likert scale, with responses ranging from "Not at all" to "Extremely." Questions corresponded to DSM-IV symptom clusters, and included re-experiencing the traumatic event (Cluster B), avoidance/numbing (Cluster C), and increased arousal (Cluster D). Although a total score of 50+ has been used in previous research as a predictor of PTSD [50], including military samples [28, 30], in the present study we screened participants according to the number of symptoms they reported in each of the three symptom clusters. Specifically, to screen positive for probable PTSD, participants had to report experiencing at least one Cluster B symptom, more than 2 Cluster C symptoms, and more than 1 Cluster D symptom.

The Patient Health Questionnaire-8 (PHQ-8) was used to assess how often depressive symptoms were bothersome over a two week period prior to attending the study. Occurrence was rated "Not at All," "Several Days," "More Than Half the Days," and "Nearly Every Day." Scores above 10 are considered a positive screen for major depression [51].

Finally, the DVBIC TBI Screening Tool [52, 53] was used to assess lifetime history of concussion. This 3-item screening tool was administered verbally by the experimenter.

Materials and Apparatus

The materials and apparatus used for eyeblink conditioning were consistent with those used in previous studies [28, 54]. The tone stimulus was produced by a custom software signal generator in MATLAB and a digital-to-analog converter (USB-6211, National Instruments), and passed through a David Clark aviation headset (Model H10-50, Worchester, Massachusetts, USA). A Realistic sound meter (Radio Shack, Fort Worth, Texas, USA) verified sound levels. Headphones provided the auditory stimuli for eyeblink conditioning, which was an 82 dB pure tone lasting 500 ms with a 5 ms rise/fall [55]. Air puffs were produced by pressurizing ambient air to 5 psi (e.g., Fürgut Industries, Aitrach, Germany), and released through silastic tubing attached to the boom of the headphones by a computer controlled solenoid valve (e.g., Clipper Instruments, Cincinnati, OH). The boom was placed 1 cm from the eye and aimed at it.

Eyeblink responses were obtained through electromyography (EMG) signal recording via pediatric silver/silver chloride electrodes coated with a conductive gel. These electrodes were placed above and below the right eye, with a ground electrode placed on the neck below the right ear. A BMA-200 isolated physiological amplifier (CWE, Ardmore, Pennsylvania, USA) was used to electronically band-pass (1 Hz to 30 Hz) and amplify the signal by a factor of 1000. The resulting signal was sampled at 1000 Hz and digitized through an analog-to-digital converter

board (USB-6211, National Instruments). The EMG signal was passed to a medically isolated physiological amplifier (UFI, Morro Bay, CA, USA), low-pass filtered and amplified 10 K. The EMG signal was sampled at 500 Hz by an A/D board (PCI 6025E, National Instruments, Austin, TX, USA) connected to an IBM-compatible computer. Stimulus generation was controlled by a custom MATLAB data acquisition program.

Procedure

For the conditioning session, participants were seated in a comfortable chair and fitted with EMG electrodes. They were instructed that the study was evaluating reflex responses to tones and puffs of air to the eye, and that they should remain awake. A silent film (e.g., a nature program) was played in the background for the duration of the conditioning session in order to maintain attention. Upon initiation of the conditioning program, participants experienced three US-alone trials in which a 50-ms, 5 psi air puffs were delivered to assess UR quality and boom adjustments. Following the US-exposure period, participants began delay conditioning. A 50% partial reinforcement schedule was used in which a 500-ms/1200 Hz pure tone CS co-terminated with a 50 ms airpuff US on 50% of the trials. The training session consisted of 60 trials. The inter-trial interval was jittered at 15-30 seconds.

Signal Processing

Electromyography data were evaluated on a trial-by-trial basis for all participants. To determine the occurrence of an eyeblink, a threshold value of .2 (unitless) was used as criteria for the peak detection function. If a peak was detected but did not exceed the threshold or a 250 ms mean of the baseline plus two standard deviations, the peak was not counted as an eyeblink response. The slope coefficients (COS 1/COS 2), representing the forward and backward facing slope of the eyeblink waveform ± 25 ms on either side of the peak, were used as an additional

criteria for a detected peak to be counted as a proper response. This value could be adjusted to shorten/lengthen the slope calculation length in order to exclude certain slow moving waveforms that may have a naturally occurring peak within a CR or UR window. To avoid being counted as a false positive identification of an eyeblink response, the slope of the detected wave had to be sufficiently high to resemble a typical eyeblink.

Data Analysis

Statistical analyses were conducted using SPSS Version 23. The rejection criterion for statistically significant results was $p < .05$, with post-hoc comparisons corrected for family-wise error using a Bonferroni correction. Corrected degrees of freedom were used for independent samples *t*-tests in the event of unequal variances between means. The primary dependent measure of interest was the proportion of CRs elicited during the acquisition period in for each personality group of interest. The 60 trial acquisition period was divided into blocks of 10 trials. The between-subjects variable for the principal analysis was personality group classification, with trial block serving as a repeated measure. For Type D, follow-up analyses compared learning as a function of the NA and SI components independently. All repeated measures data were corrected for sphericity using a Greenhouse-Geisser correction.

Results

Demographic Data

Demographic data for the entire sample are presented in Table 1 as a function of sex. Although male and female CG personnel significantly differed in age, as well as number of deployments, there were no sex differences in personality characteristics or mental health complaints (all p's > .05).

Self-Report Measures

Behavioral Inhibition. Approximately 34% (26/78) of the sample was characterized as BI. BI and Non-Inhibited personnel did not differ on demographic or service-related factors (all *p*'s > .05). In terms of mental health complaints, as shown in the left panel of Table 2, BI personnel endorsed a significantly greater number of depressive symptoms on the PHQ-8 ($t(34.1) = -2.60$, $p = .014$). Of the four cases of probable MDD (pMDD) in this sample, three of these were also classified as BI, which approached a statistically significant difference ($\chi^2(1) = 3.3$, $p = .07$). BI was also associated with greater total scores on both the PCL-M ($t(30.1) = -3.03$, $p < .01$) and PCL-C ($t(28.9) = -2.71$, $p = .011$), as well as Cluster B (PCL-C only), Cluster C, and Cluster D symptoms (all *p*'s > .05). Note that when using the symptom scoring method for screening probable PTSD (pPTSD) using the PCL, all 6 personnel that screened positive for pPTSD were also identified as BI.

To the degree that the BI classification demonstrated a high concordance with pPTSD and pMDD caseness, of interest was the degree personality was associated with symptoms in those that did not meet case definitions for psychopathology (i.e., sub-syndromal symptomology). Thus, differences in mental health complaints were assessed in BI with pPTSD and pMDD cases removed. As shown in the right panel of Table 2, when these cases were removed, BI demonstrated greater total scores on the PCL-M and Cluster D (PCL-M only), as well as a greater number of MDD symptoms.

Type D Personality. The prevalence rate of Type D personality was 18% (14/78). These rates are consistent with those reported by Mommersteeg et al [37] in an active duty Dutch military sample (15%). There were no group differences in age, sex, education, rank, number of deployments, or prior history of concussion (all *p*'s>.05). Only 7 of the 14 personnel classified as Type D were also BI; however, BI was associated with greater total scores on the DS14 ($t(35.9)$

= -3.55, p = .001), as well as greater scores on measures of NA ($t(35.4) = -2.76$, p = .01) and SI ($t(76) = -3.7$, $p < .001$). As shown in the left panel of Table 3, compared to Non-Type D, Type D was associated with a significantly greater number of depressive symptoms on the PHQ-8 ($t(13.9) = 2.83$, $p<.01$). In terms of self-reported posttraumatic symptoms, Type D expressed significantly greater total scores on both the PCL-M ($t(13.8) = -2.99$, $p = .01$) and PCL-C ($t(14.8) = -3.32$, $p = .005$). Scores on symptom Cluster C and Cluster D, but not Cluster B ($p > .10$), were significantly higher in Type D than Non-Type D for PCL-M and PCL-C. Using the symptom scoring method for PCL measures, 6 of the 78 Coast Guard personnel (8%) enrolled in the study screened positive for pPTSD. This included 5 of the 14 Type D personnel (35.7%) and only 1 of the 65 Non-Type (1.5%), a statistically significant difference ($\chi^2(1) = 18.9$, $p<.001$).

As was done in our analysis of BI, we also assessed mental health complaints when personnel screening positive for pPTSD and/or pMDD were excluded. As shown in the right panel of Table 3, total scores on the PCL-C remained significantly higher in Type D.

Eyeblink Conditioning

Inspection of eyeblink data resulted in the exclusion of 16 participants (15 males and 1 female). Two of the participants excluded met criteria for Type D personality, whereas 14 others were classified as Non-Type D. Of those participants excluded, 7 were also classified as BI. Exclusions were due to excessive noise in the EMG signal, poor attention in maintaining eyes open, or participants failing to demonstrate CR rates above spontaneous blink rates during training.

*Behavioral Inhibition***.** Acquisition rates for personnel classified as BI were examined in a 2 (Group: BI vs. Non-Inhibited) x 6 (Training Block) mixed ANOVA. Mauchly's test indicated that the assumption of sphericity had been violated ($\chi^2(14) = 39.6$, $p < .001$), therefore

Greenhouse-Geisser estimates of sphericity (ε = .78) were used to correct the degrees of freedom in the analysis. As shown in Figure 1, there was a significant main effect of Training Block ($F(3.90, 230.3) = 11.3$, $p<.001$, $\eta^2 = .16$), but not Group status ($F(1, 59) = 0.2$, $p = .676$, $\eta^2 = .01$). These effects were qualified by a significant interaction between BI and Training Block ($F(3.90, 230.35) = 2.5$, $p = .05$, $\eta^2 = .04$) indicating a greater proportion of CRs in later training blocks for BI compared to Non-Inhibited personnel.

*Type D Personality***.** As shown in Figure 2, Type D personnel exhibited a greater number of CRs across six training blocks than Non-Type D. This was confirmed in a 2 (Group: Type D vs. Non-Type D) x 6 (Training Block) mixed ANOVA. Mauchly's test indicated that the assumption of sphericity was violated ($\chi^2(14) = 43.1$, $p<.001$) therefore degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity (ε = .77). The results showed a significant main effect of Training Block ($F(3.82, 225.60) = 6.5$, $p = .001$, $\eta^2 = .10$) and a significant main effect of Group ($F(1, 59) = 8.2$, $p = .006$, $\eta^2 = .12$). The interaction between Group and Training Block was not significant ($F(3.82, 225.60) = 0.9$, $p = .498$, $\eta^2 = .02$).

As a follow-up analysis, the independent effects of NA, SI, and their interaction on learning were examined. Acquisition rates for NA personnel varied little over time (top panel of Figure 3), whereas there were pronounced differences in learning when personnel were classified as SI (bottom panel of Figure 3). This divergent pattern of learning as a function of the NA and SI personality dimensions was confirmed in a 2 (NA: high or low) x 2 (SI: high or low) x 6 (Training Block) mixed ANOVA. Note that corrected degrees of freedom using Greenhouse-Geisser estimates of sphericity (ε = .78) were used for this analysis to correct for sphericity in our repeated measures ($\chi^2(14) = 43.5$, $p<.001$). There was a significant main effect of Training Block ($F(3.84, 222.84) = 8.8$, $p < .001$, $\eta^2 = .13$), which confirmed that learning occurred as the

training session progressed. Critically, the proportion of eyeblink CRs did not significantly differ as a function of high or low NA ($F(1, 58) = 0.5$, $p = .474$, $\eta^2 = .01$), whereas there was a significant difference when comparing high and low SI ($F(1, 58) = 9.9$, $p = .003$, $\eta^2 = .15$). Specifically, high SI personnel produced more eyeblink CRs than low SI personnel, overall. The interaction between NA and SI did not reach statistical significance ($F(1, 58) = 2.5$, $p = .12$, $\eta^2 = .04$), nor were there any interactions between the personality groups and training blocks (all p's > .05).

Learning and Mental Health Symptoms

Finally, the effectiveness of learning performance as a predictor of mental health symptoms was assessed. CG personnel were classified on the basis of the number of CRs produced over the entire training period. "Fast Learners" ($N = 21$) were characterized as those personnel located in the top 1/3 of the distribution, whereas "Normal Learners" ($N = 41$) occupied the bottom two-thirds of the distribution. As shown in Table 4, learning groups differed significantly in terms personality, with Fast Learners reporting greater total scores on the DS14 (assessing Type D personality) and AMBI (assessing inhibited temperament). Critically, despite suggestive numerical differences, PTSD and MDD symptoms were not differentiable as a function of learning performance.

Discussion

Recall that the sample of active duty military assessed for eyeblink conditioning in the present study was part of a larger cross-sectional study assessing relationships between stress-related symptomology, neurocognitive performance, and biological markers. In the overall study, which comprised a total of 241 CG personnel, 15% met screening criteria for pPTSD using symptom scoring methods. In the present study, which utilized a subset of this larger

sample, 7% met symptom screening criteria for pPTSD. Similarly, there were fewer suspected cases of pMDD in this reduced sample (3%) when compared to the overall sample (6%). In the present study, BI temperament classified all suspected cases of pPTSD, whether from military or civilian trauma; BI also effectively classified comorbid PTSD/MDD, although it missed one case of probable MDD, absent co-morbid PTSD. Consistent with the full sample, BI endorsed a greater number of posttraumatic symptoms on both the PCL-C and PCL-M. As shown in Table 2, when excluding those participants meeting caseness for PTSD and MDD, BI still demonstrated greater total scores on the PCL-M and endorsed a greater number of Cluster D symptoms on the PCL-M. The inherent wariness and withdrawal of BI, indicative of hypervigilance, is consistent with Cluster D. In contrast, Type D classified 5/6 of the suspected cases of PTSD, as well as the case of MDD alone. As shown in Table 3, when excluding suspected cases of PTSD and MDD, those expressing Type D still produced greater total scores on the PCL-M than Non-Type D. Together, these data suggest that BI and Type D may be sensitive to subclinical symptoms as well as caseness of PTSD.

The critical question was whether these personality factors would also be related to positive learning biases. Consistent with previous work, BI was associated with positive learning biases, evident during the partial reinforcement schedule tested. Facilitated acquisition of eyeblink conditioning is thus apparent in those expressing BI on a continuum from civilians without a high degree of anxiety symptoms [20, 21, 23], to active duty military expressing PTSD symptoms, to veterans with PTSD [28, 30].

A more dramatic learning bias was demonstrated in those classified as Type D. Recall that the Type D designation is comprised of NA and SI components. In parsing these two components of Type D, an interesting pattern emerged. Facilitation of eyeblink CRs was largely

driven by SI, rather than NA or the NA/SI interaction. The propensities for inhibitory behavior, like those seen in SI and BI, underlie positive biases in the associative learning. On the other hand, NA lacked specificity in characterizing learning. NA is a common feature of PTSD and MDD. In contrast to faster acquisition of eyeblink conditioning in PTSD, impaired eyeblink conditioning has been reported in MDD by Greer and colleagues [45]. Using a partial reinforcement schedule, overall learning rates are expected to be modest relative to full reinforcement. Thus, we lacked sensitivity to detect poorer learning with the present set of parameters.

An overarching goal is to identify, with a biologically-driven, empirical assessment, those experiencing stress-related symptoms as precursors to PTSD and MDD. Inasmuch as acquisition of eyeblink conditioning is facilitated by acute stress exposure [56, 57], a possible classifier of stress-related symptoms would be acquisition rates. However, a learning criterion to divide those faster in acquisition from those that acquired conditioned eyeblink responses more slowly was not sensitive to pPTSD, pMDD or degree of symptoms. What was apparent was faster acquisition tended to be expressed in those personnel identified as BI and Type D. Faster acquisition may be derived from several neurobiological or attentional sources, which would not seem to be specifically related to stress-related symptoms. The conjunction of inhibited temperament with learning rates may represent a significant classifier for pPTSD.

Limitations and Future Directions

There are several limitations of the current study. First, as this work relied on a cross-sectional design, we were limited in our ability to make any causal inferences about the relationship between personality, learning, and the subsequent development of stress-related symptoms. To this end, a longitudinal design tracking active duty personnel, from early in the

induction process through active duty posting, would provide a more suitable vehicle to test hypotheses derived from the learning diathesis model of stress and anxiety. As cross-sectional studies are strictly observational in nature, it is possible that personality characterizations of active duty personnel reflected transient emotional states or tendencies, rather than personality, *per se*. As there were no assessments of personality that pre-dated the emergence of stress-related symptoms, it is difficult to determine whether the Type D and BI classifications were functioning as more state-like or trait-like constructs at the time of testing. However, with regard to distressed personality, there is evidence to suggest that, while not immutable, Type D is nonetheless temporally stable [39]. Kupper et al. report that the Type D designation demonstrated good test/re-test reliability over a 9-year period, and that the etiology of stable Type D personality caseness was primarily the product of enduring genetic factors. However, Kupper et al. also reported that environmental factors contributed to changes in caseness over time in their sample. With regard to BI, there is evidence that the avoidant temperamental style develops early in life and shows good temporal stability [24], although some individuals do change classification over time [49]. Related to this, the current study utilized a non-clinical sample in which stress-related symptoms were self-reported. As noted previously, few of the surveyed personnel met criteria for pPTSD, limiting our ability to examine the relationship between associative learning and pPTSD.

Despite these limitations, the current findings support a growing literature examining enhanced associative learning in personality dimensions associated with the development of stress and anxiety disorders, such as PTSD. Various psychosocial factors, such as personality and temperament, have been tied to positive biases in associative learning, suggesting that these factors may contribute to an increased risk of developing anxiety disorders in anxiety-prone

individuals when exposed to aversive stimuli. The learning advantage we report in Type D personality and inhibited temperament in eyeblink conditioning may offer further insight into this hypothesized pathway to dysfunction.

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Tables

Table 1.
Demographic and Mental Health Questionnaire Data for Active Duty Coast Guard Personnel as a Function of Sex.

	Males	Females	*p*-value
Age	30.39 (5.73)	24.93 (4.48)	.001
Years of Education	12.91 (1.67)	12.57 (1.45)	.49
Rank			
E1-E4	27/64	12/14	.06
E5-E6	28/64	2/14	
E7-E9	6/64	0	
Officer	2/64	0	
Deployment History			
Yes	29/56	2/14	.01
Combat Experience (CES)			
Yes	10/62	0/13	.12
History of Concussion (DVBIC)			
Yes	30/64	3/14	.08
Behavioral Inhibition (AMBI)			
Total Score	13.42 (5.70)	13.00 (5.87)	.80
Type D Personality (DS14)			
Total Score	18.13 (8.22)	20.71 (5.21)	.26
NA	8.05 (5.74)	9.14 (4.05)	.50
SI	10.08 (3.80)	11.57 (2.28)	.16
Depression (PHQ-8)			
Total Score	3.56 (4.21)	4.08 (2.10)	.67
PCL-M			
Total Score	24.08 (10.31)	25.71 (14.14)	.62
Cluster B	0.19 (0.81)	0.86 (1.66)	.17
Cluster C	0.50 (1.33)	0.50 (1.16)	.99
Cluster D	0.82 (1.43)	1.50 (1.95)	.24
PCL-C			
Total Score	26.32 (10.83)	25.79 (10.06)	.87
Cluster B	0.60 (1.17)	0.50 (1.16)	.77
Cluster C	0.87 (1.57)	0.43 (0.94)	.31
Cluster D	0.83 (1.26)	1.50 (1.99)	.24

Note: *p*-values correspond to independent samples *t*-tests for continuous values, and χ^2 tests for categorical values. *SD* is represented in parentheses for continuous values.

Table 2.
Mental Health Complaints in Behaviorally Inhibited and Non-Inhibited Personnel.

	pPTSD and pMDD Cases Included			pPTSD and pMDD Cases Excluded		
	BI	**Non-Inhibited**	***p***	**BI**	**Non-Inhibited**	***p***
PHQ-8						
Total Score	5.46 (4.93)	2.74 (2.88)	.01	4.00 (2.94)	2.49 (2.29)	.05
PCL-M						
Total Score	30.65 (14.87)	21.37 (6.61)	.01	26.55 (8.77)	21.45 (5.44)	.02
Cluster B	0.62 (1.55)	0.16 (0.58)	.16	0.30 (0.98)	0.16 (0.60)	.48
Cluster C	1.04 (1.89)	0.22 (0.70)	.04	0.45 (1.00)	0.14 (0.46)	.20
Cluster D	1.96 (1.93)	0.51 (1.16)	.001	1.50 (1.67)	0.43 (0.98)	.01
PCL-C						
Total Score	31.84 (14.65)	23.52 (6.66)	.01	27.00 (11.17)	23.37 (6.55)	.21
Cluster B	1.12 (1.64)	0.33 (0.73)	.03	0.83 (1.34)	0.31 (0.71)	.13
Cluster C	1.60 (2.16)	0.40 (0.77)	.01	0.89 (1.45)	0.35 (0.69)	.14
Cluster D	1.36 (1.66)	0.75 (1.28)	.11	0.89 (1.49)	0.73 (1.30)	.70

Note: *p*-values correspond to independent samples *t*-tests for continuous values, and χ^2 tests for categorical values. *SD* is represented in parentheses for continuous values.

Table 3.
Mental Health Complaints in Type D versus Non-Type D Personnel.

	pPTSD and MDD Cases Included			pPTSD and MDD Cases Excluded		
	Type D	**Non-Type D**	***p***	**Type D**	**Non-Type D**	***p***
PHQ-8						
Total Score	7.57 (6.26)	2.75 (2.46)	.01	4.50 (3.30)	2.68 (2.41)	.06
PCL-M						
Total Score	36.14 (17.78)	21.73 (6.56)	.01	27.88 (10.30)	22.08 (6.03)	.16
Cluster B	0.79 (1.81)	0.21 (0.75)	.26	0.13 (0.35)	0.22 (0.76)	.74
Cluster C	2.07 (2.30)	0.15 (0.47)	.01	0.88 (1.36)	0.15 (0.48)	.18
Cluster D	2.86 (2.18)	0.52 (0.95)	.001	1.75 (2.12)	0.53 (0.95)	.15
PCL-C						
Total Score	37.07 (14.46)	23.81 (7.88)	.01	31.13 (10.93)	23.42 (7.31)	.01
Cluster B	1.07 (1.49)	0.48 (1.06)	.18	0.63 (1.19)	0.42 (0.91)	.58
Cluster C	2.43 (2.41)	0.43 (0.86)	.01	1.38 (1.85)	0.37 (0.74)	.17
Cluster D	2.43 (1.79)	0.62 (1.11)	.002	2.13 (2.10)	0.59 (1.12)	.08

Note: *p*-values correspond to independent samples *t*-tests for continuous values, and χ^2 tests for categorical values. *SD* is represented in parentheses for continuous values.

Table 4.
Demographic and Mental Health Questionnaire Data for Active Duty Coast Guard Personnel Classified as Normal Learners and Fast Learners.

	Normal Learners	Fast Learners	*p*
Behavioral Inhibition (AMBI)	11.93 (5.25)	14.95 (5.84)	.04
Type D Personality (DS14)			
Total Score	16.20 (6.42)	21.95 (10.14)	.01
NA	7.03 (5.02)	10.67 (6.70)	.02
SI	9.18 (2.78)	11.29 (4.63)	.03
Depression (PHQ-8)			
Total Score	3.05 (2.72)	4.86 (5.32)	.08
PCL-M			
Total Score	23.63 (8.26)	28.61 (15.70)	.19
Cluster B	0.18 (0.71)	0.67 (1.56)	.18
Cluster C	0.30 (0.91)	0.95 (1.88)	.15
Cluster D	0.98 (1.48)	1.29 (2.03)	.54
PCL-C			
Total Score	24.69 (10.44)	28.76 (12.77)	.19
Cluster B	0.54 (1.23)	0.62 (1.16)	.81
Cluster C	0.69 (1.38)	1.00 (1.87)	.47
Cluster D	0.80 (1.32)	1.43 (1.91)	.19

Note: *p*-values correspond to independent samples *t*-tests for continuous values, and χ^2 tests for categorical values. *SD* is represented in parentheses for continuous values.

Figures

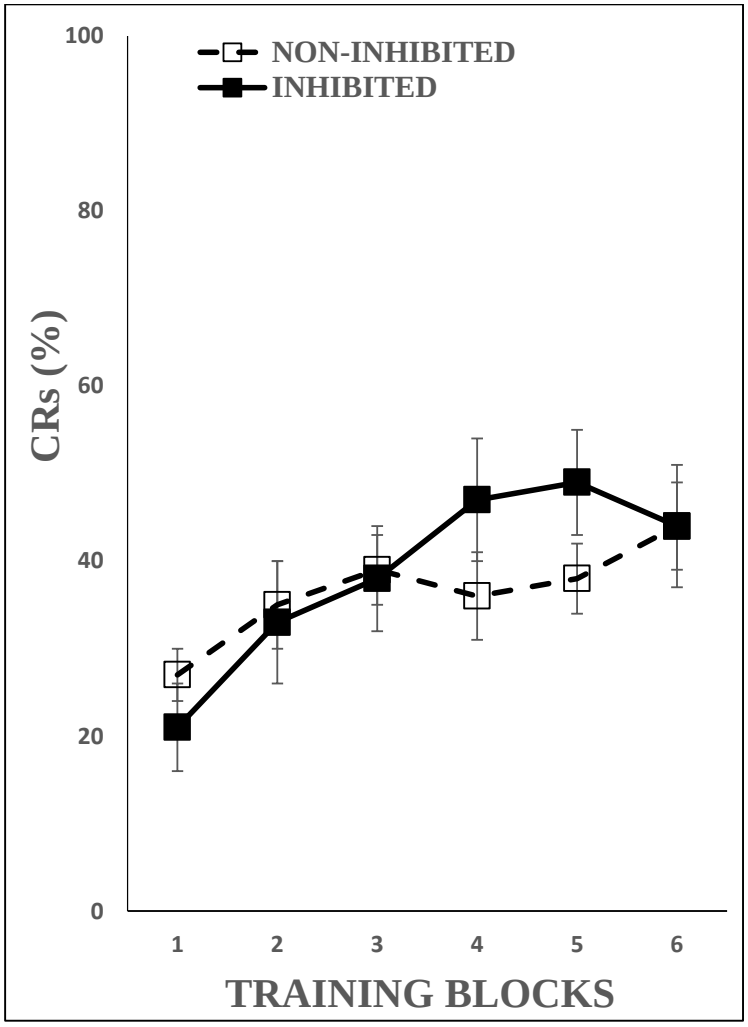

Figure 1. Proportion CRs for Behaviorally Inhibited vs. Non-Inhibited personnel over six training blocks. Note: Error bars represent ± 1 SE.

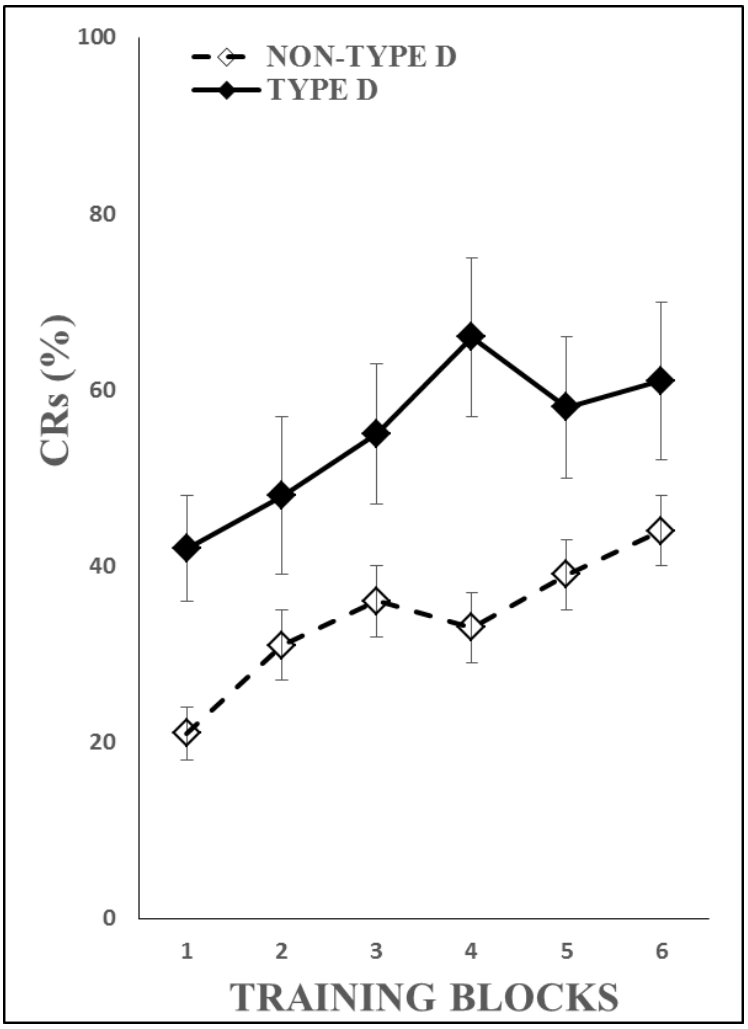

Figure 2. Proportion CRs for Type D versus Non-Type D personnel across six training blocks. Note: Error bars represent ± 1 SE

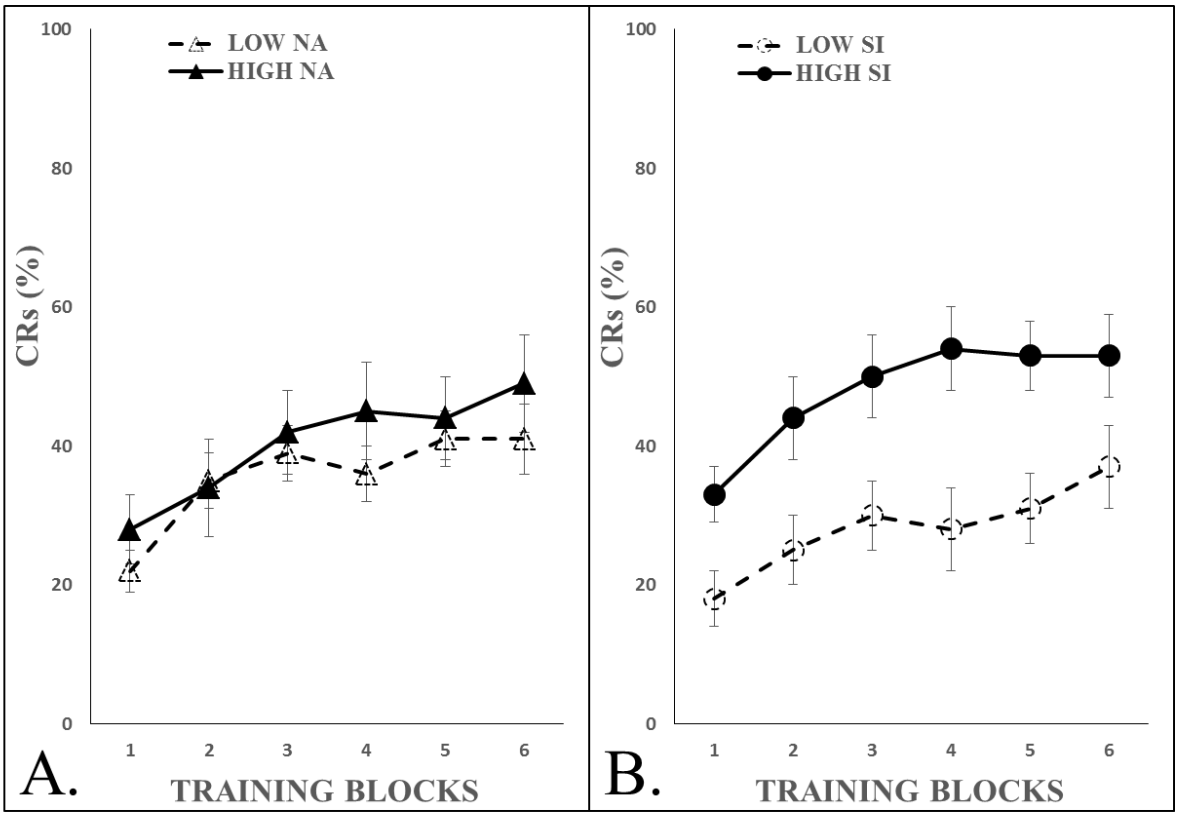

Figure 3. Acquisition data as a function of NA and SI subscales of DS14. (A) Proportion CRs for High NA vs. Low NA personnel across six training blocks. (B) Proportion CRs for High SI vs. Low SI personnel across six training blocks. Note: Error bars represent ± 1 SE.